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Mediastinal and Pulmonary Changes in Erythema Nodosum[1]

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THE ETIOLOGY of erythema nodosum has been the subject of considerable speculation. Spink (3) lists the following explanations that have been given:

1. It is a manifestation of tuberculosis.
2. It occurs as part of the symptom-complex of rheumatic fever.
3. It has its origin in streptococcic infection.
4. It is a specific infectious disease, the etiology of which is unknown.
5. It may occur during the course of various infections, and any one of a number of toxic and bacterial agents may be the cause, including the tubercle bacillus and the hemolytic streptococcus.

After discussing these various theories, and as a result of his own experience, Spink concludes that the last mentioned explanation is the correct one. In children, tuberculosis seems to be the common precipitating factor. Wallgren (5) has presented evidence in this respect, although agreeing that it is a non-specific allergic cutaneous eruption which occurs occasionally in other infections and may possibly be provoked by non-infectious agents. In children the erythema appears at the time that the child becomes tuberculin-sensitive, and Wallgren believes the fever marks the boundary between the pre-allergic stage and the stage of manifest tuberculous infection. In adults less emphasis seems to have been placed on tuberculosis as an etiologic factor and more on rheumatic fever and other streptococcic infections. Among the various diseases and agents held responsible are lymphogranuloma venereum, dental infection, chronic meningococcic septicemia, syphilis, influenza, chronic ulcerative colitis, and certain drugs such as the bromides and potassium iodide.

Recently, Dickson (1) called attention to the association of erythema nodosum and coccidioidomycosis as seen in the San Joaquin Valley of California, where it is known as the "valley fever" or "desert fever." Of interest roentgenologically is his description of the pulmonary changes seen during this disease. During the acute attack, dense shadows were found usually in the hilar regions, indicating enlargement of the hilar glands. Radiating from the hilar areas and widely distributed through the lung areas were densities indicating parenchymatous involvement of the lung. As time went on the lesions gradually cleared and the lungs usually returned to a normal appearance. Examination of the sputum and gastric contents showed that the causative agent was the Coccidioides fungus.

Keil (2), from his own observations and a critical survey of the literature, does not believe that erythema nodosum is of rheumatic origin and further states that these

[1] From the Department of Radiology and Physical Therapy, State of Wisconsin General Hospital, Madison, Wis. Presented before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

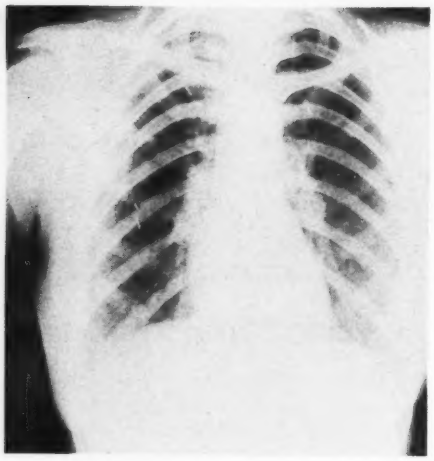


Fig. 1. Case 1. Distinct, though slight, bilateral soft enlargement of hilum lymph nodes.

cases should not be labelled as tuberculous when the tuberculin test is positive nor rheumatic when the reaction is negative.

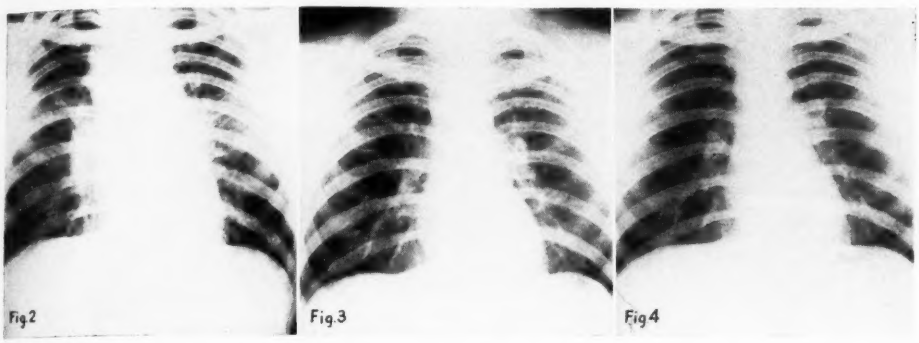
In an analysis of 133 cases of erythema nodosum, Spink found 48 with chest roentgenograms. Of these, 30 were negative; 3 revealed enlargement of the hilum lymph nodes; 2, old calcified tuberculosis of the lungs; 1, an abscess in the right upper lobe; 1, slight clouding of the left apex; and the remainder, variable findings of apparently no significance as far as the skin lesions were concerned.

In children, positive evidence of a primary tuberculous infection is found in a majority of the cases (pathologically enlarged hilum shadows and infiltration in the lung parenchyma).

In general the consensus of opinion may be said to be that there is no one specific infection or toxic agent responsible for erythema nodosum. In children, and this is especially true in the Scandinavian countries, the majority of cases are due to tuberculosis. In adults the problem is by no means settled and there seems to be no general agreement except that most observers feel that no one specific agent is responsible.

Because the pulmonary roentgenologic aspects and the value of roentgen examination of the lungs have not been particularly stressed, and since the roentgenologic literature is especially devoid of mention of this disease, a series of cases in which roentgen examination of the lungs was done has been reviewed and this material forms the basis for the present communication.

Among 42 patients admitted to the State of Wisconsin General Hospital with a diagnosis of erythema nodosum, there were 20 who had roentgenograms of the chest. All of these patients except one were adults. In 8 cases the chest roentgenograms were entirely negative for evidence of present or past disease. The remaining 12 showed varying degrees of pathologic change. In one there was an apical pleural cap with a minimal amount of subpleural parenchymal density. Three examinations of the sputum were negative for tubercle bacilli and the intradermal tuberculin test was negative. The relationship of the pleural and pulmonary changes to the erythema nodosum is, therefore, highly doubtful. Another patient had typical erythema nodosum in 1932. No chest roentgenogram was made at that time. Two years later she developed a tuberculous pleural effusion, followed by the appearance of parenchymal lesions and the sputum became positive for tubercle bacilli. She received active treatment for tuberculosis and at the last report, one and one-half years ago, still had active disease. It is unfortunate that no chest film was made at the time of the erythema nodosum, and one can only speculate as to the relationship of this disease and the later development of active tuberculosis. It is possible that the erythema nodosum represented the development of allergy to tuberculoprotein and that the pleural and parenchymal tuberculosis was of the reinfection type, but there is no proof for this assumption. Another patient showed only an apical pleural scar. The Mantoux test was negative. The remaining 9 cases showed varying degrees of hilum lymphadenopathy and will be considered in more detail. Of these 9 cases, 3 showed slight but definite



Figs. 2–4. Case 2. Figure 2 shows the appearance of chest at the height of the disease. Generalized enlargement of mediastinal and hilum lymph nodes is evident together with soft striation into the adjacent lung fields. Note particularly the sharply outlined mass in the right paratracheal area.
Figure 3 shows the appearance of chest eight months later, when most of the adenopathy has disappeared.
Figure 4 is the final roentgenogram, taken one year later than Figure 2.

degrees of hilum enlargement of nodular type. The other 6 showed moderate to pronounced changes in the hilum shadows.

The following case is illustrative of the group showing slight hilum enlargement.

Case 1 (A. K.): A white female, age 38, was admitted on Nov. 11, 1937, complaining chiefly of pain and swelling of the ankles. For three weeks prior to admission she had suffered from aching and pains in the legs and thighs. Painful, red, swollen areas had appeared on both legs. There had been no fever or malaise. Of interest in the past history was the record of four attacks of pyelitis since 1925. These had been accompanied by high fever, urinary frequency, and dysuria. The weight had been stationary.

Both ankles were swollen, hot, and tender. There were red, tender nodules up to 4 cm. in diameter on both legs, especially the extensor surfaces. The clinical diagnosis was erythema nodosum and pyelitis. The intracutaneous tuberculin test was negative with 0.01 mg. of old tuberculin and again with 0.1 mg. A roentgenogram of the chest revealed a slight but definite soft nodular increase of both hilum shadows. The chest was otherwise normal (Fig. 1). There has been no follow-up of the chest roentgenogram.

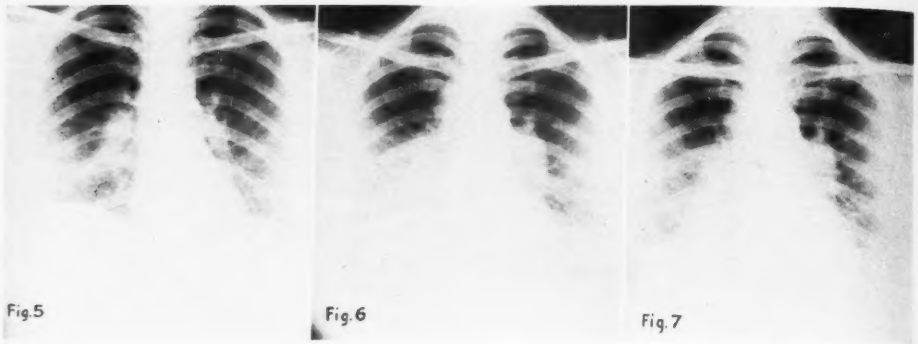
Comment: The changes shown in the film are slight but still more than should normally be present in a patient of this age. Such slight degrees of hilum lymphadenopathy are not specific, however, for any one disease, and in this instance they may well have been due to a non-specific inflammatory reaction. The other two cases in this group showed similar appearances. It is entirely possible that the changes noted in the roentgenograms had no relationship to the erythema nodosum, but because we believe the roentgenograms were not normal they have been included. In none of the three cases have follow-up studies been made.

Of greater interest and importance are the cases listed as showing moderate to pronounced hilum and mediastinal lymph node enlargement. The following are representative of this group:

Case 2 (R. H.): A white male, age 24, was first admitted to the hospital on Feb. 9, 1935, with "bunches on the feet." His present trouble had begun with an acute upper respiratory infection about two months previously. A dry, irritating cough had persisted and had become progressively worse. About a month previous to admission painful nodules had appeared over the ankles and shins associated with stiffness in the ankles. The appetite was poor. No weight loss had been noticed.

The patient appeared acutely ill. The temperature was 101°, pulse 96. There were coarse inspiratory and expiratory râles in the chest, and a systolic apical shock with a short systolic murmur at the cardiac apex. The inguinal lymph nodes were palpable bilaterally. Numerous tender red nodules were present on the shins and extensor surfaces of both legs and arms. The blood count on admission revealed 13,100 white blood cells with 80 per cent neutrophiles. Three weeks later the count was normal. A roentgenogram of the chest demonstrated a considerable widening of the supracardiac shadow, especially to the right, and a marked increase in density and extent of the hilum shadows. There was a soft thickening of the peribronchial trunks, especially in the left mid-lung field (Fig. 2).

The acute symptoms subsided after twelve days,



Figs. 5–7. Case 3. Figure 5 is the roentgenogram of the chest at the time of first admission, March 30, 1938.

Figure 6 was taken June 23, 1938. The disease has shown considerable advance. Microscopic examination of material removed from the right main bronchus revealed hyperplastic tuberculosis.

Figure 7, taken July 7, 1938, shows very little change.

and the patient was discharged with the following diagnoses: (1) erythema nodosum, (2) acute upper respiratory infection, (3) bronchitis, (4) conjunctivitis (5) aphthous ulcer, (6) enlargement of mediastinal and tracheobronchial lymph nodes, etiology unknown.

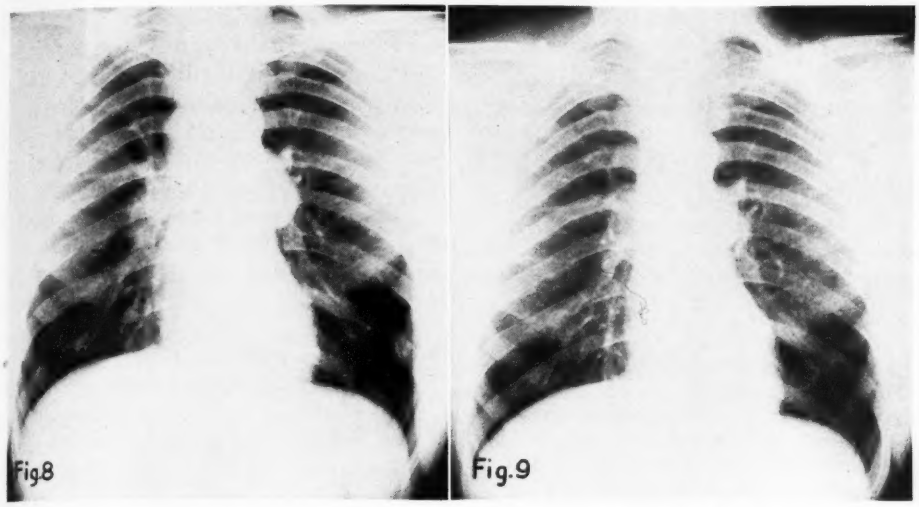
The patient was readmitted on June 7, 1935, about three months later. He felt well but continued to have chronic cough, violent at times, and occasional hemoptysis in the morning. The eyes were frequently sore, there was dyspnea, and there had been a weight loss of 30 pounds. Only one erythema nodule remained. The anterior cervical nodes were barely palpable. Seven sputum examinations were negative for tubercle bacilli. With a presumptive diagnosis of lymphoblastoma, a test series of deep roentgen therapy was given to the anterior and posterior mediastinum, consisting of four daily doses of 150 r (in air), half value layer in copper 1.0 mm.

Following this, the patient was discharged and readmitted one month later. He had shown some improvement, clinically, during the interval. Four more sputum examinations gave negative results. The cervical nodes were definitely enlarged and one was removed for histologic examination. This was reported as showing hyperplastic tuberculosis. Seven daily treatments of 200 r (in air) to the anterior and posterior mediastinum were given before the histologic diagnosis had become available. The course of the disease demonstrated roentgenologically is well shown by Figures 2, 3, and 4. At the last examination, on April 20, 1936, only slight residues of the previous changes were present (Fig. 4). A letter from his physician states that the patient is at the present time in good health. There has been no aggravation of his former trouble.

Comment: This case is of particular interest for several reasons. The illness began with an acute upper respiratory infection but it was the erythema nodosum which caused the patient to seek attention and this was the primary diagnosis at the time of his first admission. Roentgenograms of the chest showed a pronounced enlargement of the hilum and mediastinal nodes and some form of lymphoblastoma was considered as the most likely diagnosis. Numerous examinations of the sputum were negative for tubercle bacilli and a therapeutic test with radiation was deemed advisable. It was not until the cervical nodes became enlarged and one of them could be removed that the correct diagnosis of tuberculosis was established. The patient improved rapidly and at the present time, five years later, is apparently in good health. In retrospect the relationship between the erythema nodosum and the lymphadenopathy is obvious.

The next case is similar.

Case 3 (P. H.): A colored female, age 45, was admitted to the hospital on March 28, 1938, with "pains in the legs" of three weeks' duration. The pain was steady, dull, and aching in character. There were increased fatigability, some dyspnea on exercise, and a weight loss of 10 pounds. Painful reddish nodules were present on both legs. The submaxillary and cervical nodes were palpable bilaterally. Routine laboratory studies gave essentially negative results. The tuberculin test was doubtfully positive with 0.1 mg. of old tuberculin. A chest roentgenogram (Fig. 5) revealed a soft nodular shadow in the right hilum and a similar



Figs. 8 and 9. Case 4. Figure 8 is the roentgenogram of the chest at the time of admission, Feb. 25, 1935. Figure 9 shows the appearance on June 18, 1935. There has been a considerable decrease in the mediastinal masses.

but less marked change in the left. There was some calcification in the left hilum. The patient was discharged on April 6 with a diagnosis of erythema nodosum. Secondary diagnoses were dental caries, hypertrophied tonsils, varicosities of the thighs, menopausal syndrome, and obesity.

The patient was readmitted six weeks later. She said she had contracted a cold after leaving the hospital and had had it continuously for the past six weeks. The weight loss had increased to 25 pounds. The temperature showed an elevation up to 100°. Three sputum and three gastric content examinations were negative for tubercle bacilli. The Mantoux test was slightly positive with 0.01 mg. of old tuberculin. Roentgen examination of the chest (Fig. 6) showed a marked increase in the mediastinal and hilum nodes with a large soft opacity in the right medial lung base merging above with the hilum. The right paratracheal nodes were involved.

Because of the possibility of bronchial malignancy, bronchoscopic examination was done. A granular mass was found in the right main bronchus and some of it was removed. The histologic diagnosis of this tissue was hyperplastic tuberculosis. The patient was referred to a sanatorium. A final roentgenogram of the chest at the time of discharge from the hospital on July 7 showed no change in the mediastinal shadows but the opacity in the right lung field had decreased slightly (Fig. 7).

The patient was admitted a third time on Nov. 8, 1939. She had been in a tuberculosis sanatorium from July 1938 to June 1939 and had been discharged as non-infectious. She returned to this hospital for tonsillectomy. The tonsils were removed and on histologic examination showed hyperplastic tuberculosis. No roentgenogram of the chest was obtained at this last admission.

Comment: In many respects this case is similar to the previous one. At the time of the first admission the chief complaints were referable to the erythema nodosum and the mediastinal changes were found incidentally. The question of bronchial tumor was raised at the time of the second admission and on bronchoscopic examination, hyperplastic tuberculous bronchitis was discovered. The patient's subsequent course was satisfactory, but a year and a half later the tonsils were found to be the site of hyperplastic tuberculosis. Again, on review, it is obvious that the erythema nodosum was a manifestation of the tuberculosis, and the necessity for close follow-up studies of all patients with erythema nodosum, regardless of age, is apparent.

Case 4 (V. S.): A white male, age 41, was admitted to the hospital Feb. 25, 1935, with "pain in the feet." In 1930 he had a febrile attack for two weeks with an elevation of temperature up to 104°. The nature of this disease was uncertain. In November 1934 he began to have pain in the feet with some swelling. A month later (two months before admission) painful, red, swollen bumps appeared on both feet and legs with occasional similar

swellings on the hands and arms. Severe night sweats occurred. This phase lasted about two weeks and the patient had since felt weak and complained of dyspnea and palpitation on exertion.

Physical examination showed the thyroid to be enlarged and somewhat nodular The lungs were clear There was a systolic thrill at the cardiac apex and a roughening of the apical first sound with an occasional soft systolic murmur. Some pigmentation was present at the site of the previous nodules. Routine blood studies showed a mild secondary anemia and a white blood count of 15,700. Blood culture was negative after six days. Roentgenograms of the chest (Fig. 8) demonstrated a bilateral, soft, nodular thickening of both hilum shadows and an oval mass, sharply defined, overlying the pulmonary arch. The right paratracheal nodes were involved. Because of the possibility of lymphoblastoma, a test of roentgen therapy was tried, four daily treatments of 150 r (in air) to the anterior and posterior mediastinum being given. The patient was then discharged and readmitted on April 29, 1935. He said he had felt fairly well, although he still became easily fatigued. His weight had been stationary. Roentgen examination of the chest showed the mediastinal mass to have become slightly smaller. The last roentgen examination, June 18, 1935, showed a further decrease in the larger mass on the left, while the right side of the hilum had become normal (Fig 9). No further follow-up was obtained.

Comment: The chest roentgenograms revealed findings highly suggestive of some form of lymphoblastoma and, because of this, roentgen therapy in conservative doses was given. There was progressive improvement, but the final result is not known. While no proof of the nature of this process was obtained, we believe that it was tuberculous. The onset of the disease was associated with an erythema nodosum, and the combination of this disease and the pronounced lymph node enlargement in the mediastinum would seem, in all probability, to establish the diagnosis of tuberculosis.

The remaining cases were of similar type and will not be reviewed in detail.

DISCUSSION

From a roentgenologic standpoint, all of these cases offered a problem in differential diagnosis, while a scrutiny of the records shows that the same difficulty was encountered by the clinical staff as far as the mediastinal lymphadenopathy was concerned. In every instance the primary diagnosis was erythema nodosum and in some the mediastinal changes were not suspected clinically. In only two patients was it possible to establish proof of the tuberculous nature of the adenopathy. In retrospect it seems probable that all of them belonged in this category. In none of the records is there evidence that the erythema nodosum and the hilum adenopathy were considered to be associated. Lymphoblastoma was the tentative diagnosis in two and these received test doses of deep roentgen therapy, both showing improvement. In regard to Case 2, we wish to point out that in the second series of treatments a higher dose was unintentionally administered than we would care to give in a patient with tuberculous lymph nodes in the mediastinum. No harmful results could be noted, however, since the patient remained well during a five-year observation period following therapy.

These cases again demonstrate the difficulty of distinguishing between inflammatory and neoplastic mediastinal masses. It would seem, therefore, that in a given case of mediastinal and hilum enlargement, the presence of a co-existing or recent erythema nodosum should be of great value in establishing the nature of the adenopathy since, even in adults, such a combination is most likely to be of tuberculous etiology. Conversely, when roentgen examination of the chest in a patient with erythema nodosum demonstrates hilum adenopathy, the tuberculous etiology of the former can be surmised (exclusive of those cases occurring in areas where coccidioidomycosis is known to be prevalent). It is suggested, therefore, that all patients with erythema nodosum be subjected to roentgen examination of the chest as a part of the diagnostic study. Even where this is negative, follow-up examinations should be done before the patient is considered to be free from tuberculosis.

It is recognized that the chief cause or causes of erythema nodosum may vary in

different countries or in different parts of the same country The high incidence of what seems to be an associated hilum tuberculosis in our series may be explained by the fact that most of the patients admitted to this hospital come from farming or rural areas, where the incidence of negative tuberculin reactors in the adult population is known to be higher than in the more thickly populated and urban areas in the East (4). It would be expected, therefore, that more adults might be seen with hilum lymph node involvement than would be likely in institutions admitting chiefly city dwellers. On the other hand, the number of cases in our series is too small to be of statistical value, and this relative incidence of mediastinal pathologic change might not hold true if the number of cases were larger.

Recently, Widmann, Ostrum, and Fetter (6) reviewed the subject of hyperplastic mediastinal tuberculosis on the basis of 65 cases. The high incidence of colored patients in their series is noteworthy. Their observations would seem to indicate that this form of tuberculosis in adults is becoming more frequent generally. No mention of erythema nodosum as a complicating factor is made. We do not wish to indicate that we believe that all or even most cases of erythema nodosum in adults are of tuberculous etiology; that is a problem that must be worked out largely on clinical grounds. We do want to call attention to the fact that not every adult with erythema nodosum need have a streptococcic or rheumatic background for the skin lesions, and that a knowledge on the part of the roentgenologist that a given patient showing an unusual mediastinal mass has an associated erythema nodosum may make an otherwise difficult diagnostic problem easier.

SUMMARY

1. In a group of 20 patients (all but one of whom were adults) admitted with a diagnosis of erythema nodosum, for whom chest roentgenograms were made as a part of the diagnostic study, 12 showed varying degrees of mediastinal or pulmonary pathology.

2. In 3 cases these changes were minor and probably not significant. In 3 others slight but definite degrees of hilum lymphadenopathy were demonstrated. In 6 cases moderate to pronounced hilum enlargement was present.

3. Hyperplastic tuberculosis was the proved etiological factor in 2 cases of the group. In at least 4 others tuberculosis was believed to be the cause of the erythema nodosum and the hilum lymphadenopathy.

4. The theories as to the etiology of erythema nodosum are briefly reviewed. The importance of considering tuberculosis as a causative factor in this disease in adults is stressed, and chest roentgenograms and follow-up studies are recommended in all cases.

5. Radiation therapy has a place in the treatment of hyperplastic tuberculous hilum and mediastinal lymphadenopathy.

6. A knowledge on the part of the roentgenologist that a patient with nodular enlargment of the hilum and mediastinal nodes has or has had an associated erythema nodosum may make an otherwise difficult diagnostic problem easier.

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Intrathoracic Manifestations of the Lymphomatoid Diseases[1]

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IN THE LYMPHOMATOID diseases—Hodgkin's disease, lymphosarcoma, the chronic leukemias, and mycosis fungoides—success in palliation depends upon treatment of the deeply situated lesions as well as those which are superficial.

For many years, the deep, obscure pathological processes have been reported as common findings at autopsy. Many of the lesions observed at necropsy are not readily demonstrated clinically. The frequency with which such sites as the gastro-intestinal tract, the skeletal system, the genito-urinary tract, and respiratory tract are affected by the lymphomatoid diseases is not well recognized. Although the internal processes are described or mentioned in many reports, there is still a tendency to restrict treatment largely to palpable or visible evidence of disease.

In the literature of the past twenty years, sporadic references may be found to the high incidence of pulmonary and pleural involvement in the diseases under discussion. In these reports, greater emphasis has been given to the occurrence of these lesions in Hodgkin's disease. Similar pathological processes, however, are almost as frequently encountered in lymphosarcoma and lymphatic leukemia.

The purpose of this presentation is to call attention to the frequency of intrathoracic manifestations of the lymphomatoid diseases, particularly of lesions other than the ordinary mediastinal or hilar adenopathies. The survey comprises all cases with proved pathological diagnoses seen in the Memorial Hospital from 1917 to 1940, excluding current cases. Two sets of figures are recorded: one for roentgen findings, the other for autopsy findings. There are no autopsy studies for mycosis fungoides.

[1] Presented before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

Table I shows the cases studied and the grouping of cases reviewed. Totals discussed represent the grand total of 1191 cases minus (*a*) all those that were lost to follow-up, (*b*) those without roentgenographic examination of the chest, and (*c*) those in which biopsies were not fully confirmed; 794 cases were acceptable for roentgenographic study and 160 cases for an analysis of necropsy findings.

TABLE I: CASES SURVEYED FOR INTRATHORACIC LYMPHOMATOID LESIONS (MEMORIAL HOSPITAL SERIES)

	Positive Biopsy	Autopsy
Hodgkin's disease	411	51
Lymphosarcoma	372	55
(*a*) Lymphosarcoma (350)		
(*b*) Brill-Symmers (14)		
(*c*) Malignant lymphocytoma (8)		
Lymphatic leukemia	261	31
(*a*) Lymphatic leukemia (224)		
(*b*) Leukosarcoma (5)		
(*c*) Pseudo-leukemia and aleukemic leukemia (32)		
Myelogenous leukemia	133	23
Mycosis fungoides	14	0
TOTAL	1191	160

The autopsy material shows the incidence of intrathoracic lesions to be much higher than was indicated by roentgenography. This discrepancy might be reduced by more frequent roentgen examination of the chest.

The similarity of roentgen findings in these diseases would indicate that the gross pathological changes are similar. The frequency of a mediastinal mass or discrete nodes at the roots of the lungs is well recognized. This type of intrathoracic process is analogous to enlargement of superficial nodes.

The radiographic features lend themselves to analysis in the following subgroups, as differentiated by Wessler and Greene (60): (1) mediastinal tumor; (2) infiltration into the parenchyma; (3) isolated nodules in the parenchyma; (4) discrete nodes at the roots of the lungs. We

add two further subgroups: pleural thickening and pleural effusion.

HODGKIN'S DISEASE

Wessler and Greene called special attention to an enlargement of the right paratracheal nodes in Hodgkin's disease. This finding was so frequent (50 per cent) in their series of 25 cases, as compared to its occurrence in other conditions, that they believed it might be of importance in making a differential diagnosis when no node is available for biopsy. In children, however, the paratracheal nodes are frequently involved in tuberculosis, so that in this age group at least their enlargement could not be taken as diagnostic of Hodgkin's disease. In our series we did not notice any particular frequency of enlargement of the right paratracheal nodes.

Infiltrations into the lung parenchyma extend out from the hilus, producing somewhat the appearance of the peribronchial thickening and diffuse clouding of the lung fields seen in bronchopneumonia. Lemon and Doyle (28) state that Hodgkin's disease is to be suspected when the roentgenogram reveals a bilateral feathery shadow passing outward from each hilus, but other conditions such as Boeck's sarcoid, tuberculosis of the tracheobronchial nodes, and metastatic carcinoma may give similar pictures. Lenk (29) observes that the clinical picture of tuberculosis in conjunction with the roentgen picture of malignant lung tumor speaks for a diagnosis of Hodgkin's disease.

A rare type of lesion—isolated nodules simulating tumor metastases in the lung—is almost invariably found to be accompanied by one or more of the other types of intrathoracic manifestations in the lymphomatoid diseases. Wessler and Greene believed that these represent foci developing in pre-existing lymphoid tissue in the parenchyma and do not represent true metastases (Fig. 1).

When, however, one compares these round circumscribed masses as seen in the roentgenogram with sarcomatous metastatic foci from other sources, one is impressed by their similarity. We believe that the metastatic nature of some of these isolated foci cannot be dismissed when considering the fact that the Hodgkin's process must be disseminated through the body, either through the blood or lymph channels, to reach the bones and nervous system, which are grossly devoid of lymphoid elements. Undoubtedly the great majority of these circumscribed nodules do originate *in situ*, in the diffuse lymphoid stroma of the lung. But to explain a multiplicity of these nodules or the miliary foci of Hodgkin's disease, the embolic theory of origin is warranted, as in analogous processes in tuberculosis. In those cases in which the histologic picture is that of Hodgkin's sarcoma, true metastases undoubtedly occur.

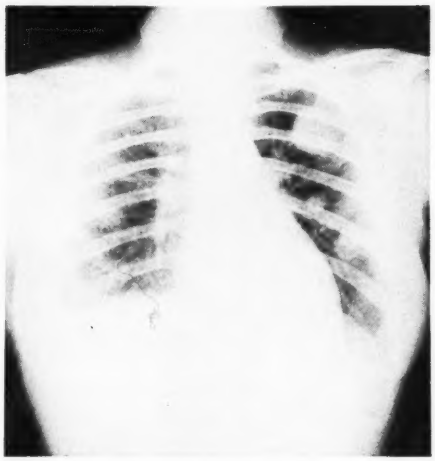

Fig. 1. Circumscribed isolated nodules in left lung in Hodgkin's disease.

In Table II is presented a comparison of our findings with reports of certain other authors (2, 12, 23, 24, 26, 41, 60, 61, 63). Our figures, compiled from a study of 335 cases, are as follows: mediastinal tumor 47.4 per cent; infiltration into the parenchyma of the lung 38.5 per cent; isolated nodules (the rarest type) 5.3 per cent; discrete nodes at roots of lungs 23.8 per cent, a lower figure than that shown by other authors; pleural thickening 7.4 per cent; pleural effusion 15.8 per cent.

TABLE II: ROENTGEN FINDINGS IN HODGKIN'S DISEASE

Author	No. Cases	Mediastinum (per cent)	Infiltration (per cent)	Isolated Nodules (per cent)	Discrete Nodes at Roots (per cent)	Pleural Thickening (per cent)	Fluid (per cent)
Kirklin and Hefke	40	60	30	12	32	...	7
Wessler and Greene	25	32	16	16	68	...	...
Baldridge and Awe	14	...	50	...	...	...	...
Whitaker	40	55	27	0	82	...	...
Kasabach and McAlpin	251	30	...	...	...	...	...
Krueger and Meyer	60	80	...	...	...	...	...
Wright	60	95	35	...	...	...	28
Falconer and Leonard	29	...	31	3 (miliary)	...	...	...
Peirce, Jacox, and Hildreth	198	37.9	13.6	...	...	11.1	...
Craver and Vieta	335	47.4	38.5	5.3	23.8	7.4	15.8
			38.5				

The term discrete nodes at the roots of the lungs as used here refers to actually discrete nodes or masses at the hilar areas. Cases in which there was a hilar thickening of any questionable interpretation whatever were not taken as representative of this type of lesion, even though distinct mediastinal disease might be present. Our hesitancy to interpret some of these shadows at the roots as discrete nodes may account for the lower percentage in our series as compared to others. The discrepancy between the incidence of these lesions on roentgenography and postmortem (Tables II, III, IV, V) in Hodgkin's disease, 23.8 and 39 per cent, and in lymphosarcoma, 11 and 25 per cent, is quite large. At postmortem, however, the affected nodes found at the hilum were often small and in our opinion could not have cast a shadow of sufficient size to enable the radiologist to make a correct diagnosis. Review of films of those patients autopsied verified this observation in many instances.

A combination of the various types of lesions is the rule in Hodgkin's disease, as stressed by most writers. We wish to emphasize the frequency of pleural effusions in this series. We have been impressed by the lack of symptoms accompanying moderate effusions in Hodgkin's disease. The question may readily arise as to how frequently previous diseases may account for pleural thickening. The frequency of infiltration in the pleura as found at autopsy (29 per cent) must, however, be noted.

From a roentgenographic analysis we have been impressed by the frequency with which intrathoracic structures are involved in the Hodgkin's process. The protean features of the lesions, however, lead to the conclusion that there are no specific roentgenologic features. The roentgenologist, at best, can make only a presumptive diagnosis of lymphomatoid disease (8, 19, 24).

Anatomists (33, 46) have established the abundance of lymphoid tissue in the pulmonary parenchyma. This lymphoid tissue is most abundant about the bronchial tubes, at the points of branching of the bronchi. It is especially concentrated between the cartilage and muscular coat of the bronchial wall. Lymphoid tissue is also found in the peribronchial connective tissues in juxtaposition to the same points of anastomosis of the bronchioles, and is present in the walls of the alveoli. The subpleural connective tissue appears to be devoid of it (15, 38). It is reasonable to expect this lymphoid tissue within the lung to be just as susceptible to the etiological factor which causes the formation of the classical lesions of Hodgkin's disease as lymphoid tissue found elsewhere. Indeed, at times in the lymphomatoid diseases, the entire diffuse lymphatic system seems to react as a whole to the exciting agent.

Estimates of frequency of primary lesions of Hodgkin's disease in the lung vary from the statement that they are fairly common to that of Terplan (52, 53), that primary foci within the lung are so rare that it is difficult to draw conclusions as to the pulmonary relation of the disease. In our experience the lungs are probably more often invaded than any structure with the exception of the lymph nodes. We do not believe any conclusion can be drawn as to frequency of lung involvement depending on the distribution of diseased nodes, *i.e.*, abdominal or mediastinal. It is quite probable, however, that the lung is more frequently involved when the predominant manifestation of the disease is in the mediastinum. In this area a transpleural spread into the lung may be effected by extension of the disease through the capsule of the nodes and into the parenchyma.

Versé described five groups of Hodgkin's lesions in the lung: (1) mediastinobronchial node lesions with direct invasion of the lung (*a*) by way of the hilum, (*b*) through the medial surface of the lung; (2) mediastinobronchial node lesions with peri- and intrabronchial spread; (3) more or less lobar (diffuse) infiltration of the lung with varying degrees of involvement of the bronchomediastinal nodes; (4) confluent lobular isolated circumscribed foci with bronchomediastinal nodes; (5) miliary (lymphohematogenous) foci with involvement in varying degrees of the bronchomediastinal nodes.

Foulon (16) believes that the alveolar tissues are directly concerned in the formation of Hodgkin's lesions. He holds that under certain circumstances lymphogranulomatosis is not an affair of the lymphoid tissue alone, but that the lesions may arise in certain cells such as the Kupffer cells of the liver and the alveolar cells of the lung. This conforms to the view of many investigators who believe that Hodgkin's disease affects the mesenchymatous tissues of the body wherever found.

Moolten (38) in his study emphasized the point that Hodgkin's disease is a "primary inflammatory reaction of granulomatous character composed of a specific cell mixture." His sections show that the Hodgkin's specific process may extend along the natural air passages, especially in the pulmonary alveoli, where the granulomatous process may grow in "pure fashion" unhampered by stroma and other tissue elements, thus producing a "pure lesion" which, nevertheless, has a specific cell mixture of varied composition including fibroblasts, histiocytes, and cells which have migrated from the blood (38, 48). In places the alveolar lumen is filled with granulomatous tissue; elsewhere the cells of the granuloma grow into masses of retracted fibrin strung from one alveolus to the next; in still other areas the fibrin masses become organized by ordinary fibroblasts and subsequently assume the aspects of a specific granulation tissue.

Versé believes that in probably more than 10 per cent of cases with pulmonary involvement, clinical and pathological evidence would lead to the conclusion that the Hodgkin's process was primary in the lung parenchyma.

Terplan considered primary lymphogranulomatosis within the lung so infrequent that conclusions concerning a lung primary lesion could not be made. He used the term "primary infect" in the same sense as Ghon tubercle. This "infect," along with the known involvement of the tracheobronchial nodes, suggests the "primary complex" of Ranke in tuberculosis. Urchs (54) believed three stages to be characteristic of Hodgkin's disease: (1) primary focus, probably in the lung, (2) generalization by lymph and blood streams, (3) tertiary lung disease by dissemination through the bronchi. These hypotheses are not illogical if one accepts Versé's concept that in approximately 10 per cent of the cases of Hodgkin's disease of the lung the primary lesion is pulmonary. This point of view has many adherents, especially among those who picture Hodgkin's disease as analogous to tuberculosis. Indeed, all lesions found in the brain, bone, skin, etc., may arise, as do similar foci in

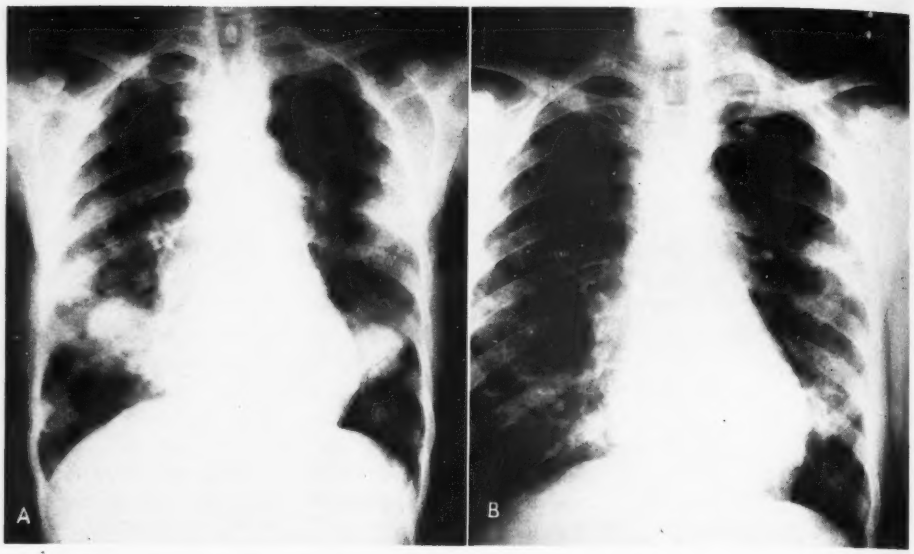

Fig. 2. Circumscribed isolated masses bilaterally in Hodgkin's disease, before (A) and after (B) treatment. Infiltration of the parenchyma is also seen.

tuberculosis, by the dissemination of "infected" emboli or the unknown etiologic agent of Hodgkin's disease rather than by a true metastasis.

In the 335 cases observed clinically and pathologically in our series, we did not find a single case in which we could definitely say that the lung parenchyma was primarily involved and other manifestations were secondary. In about 7 per cent of our cases, however, the first roentgenogram of the chest showed mediastinal, hilar, or lung parenchymal involvement.

If this observation is correct, the portal of entry of this disease may sometimes be in the respiratory tract, and in those rare cases in which isolated foci are found in the gastro-intestinal tract, the portal of entry here, as in tuberculosis, may be either the gastro-intestinal or the respiratory tract (51). Naturally these speculations must be held in abeyance until a definite etiological agent has been isolated. Recent work by Wise and Poston (42, 62) showing the co-existence of *Bacillus melitensis* with Hodgkin's disease may add to our knowledge concerning the pathogenesis in some cases.

Many authors (55, 38) stress the spread in the lung by a combination of the intrabronchial and the peribronchial types of parenchymal granulomatous infiltration. Thus the pulmonary spread takes the form of panbronchitis, involving a combination of granulomatous bronchitis and peribronchitis, or extension into the lung by radiating bands following the interlobular lymphatics as a lymphadenitis and perilymphadenitis.

In reviewing our own material we have found it difficult at times to draw a distinction in the method of spread of the Hodgkin's tissue within the parenchyma. We believe the parenchymal spread is usually the result of a combination of various types of extension. This is especially true when the infiltration is more or less lobar in character. Eleven of 51 cases fall into this classification, resulting from a peribronchial or intrabronchial spread (Table VII).

Formation of confluent lobular foci occurred in 16 of the cases in our series, but in 10 of these we found these lesions occurring as circumscribed foci alone, without any other type of involvement of the

lung parenchyma. In 7 of these 10 cases there was involvement of the hilar or mediastinal nodes. Thus in only 3 cases of this group was the formation of nodules of Hodgkin's tissue within the parenchyma the only manifestation within the thorax. In 2 of these cases the histologic picture showed a classical granuloma; in the other the histology was that of Hodgkin's sarcoma. In those cases in which isolated nodules were recognized roentgenographically (5.3 per cent) there was in each case a combination with another type of infiltrative parenchymal lesion (Figs. 2-*A* and 2-*B*). Whether these isolated foci represent metastases in the strict use of the term or represent foci of Hodgkin's tissue developing in pre-existing aggregates of lymphoid tissue of the lung or in the intrapulmonic lymph nodes, is a question which cannot be settled with our present understanding of this disease (60). The latter explanation would seem more likely to conform to all the facts as we now understand them except in rare instances in which the histologic picture is that of Hodgkin's sarcoma. These bulky intrapulmonary nodules may be sharply defined if limited by a peripheral condensation of tissue forming a pseudo-capsule, or poorly outlined if the "capsule" has been broken through. In our cases these nodular foci were represented by lesions of both types; the majority, however, had radiating fine infiltrations into the parenchyma from the solid circumscribed foci.

Having regard to intrabronchial spread of Hodgkin's disease, we have observed 5 cases in which definite ulcerations or plaques of granulomatous tissue were found in the larger bronchi. Lymphoid tissue, diffuse and in follicles, often with typical germinal centers, normally occurs regularly in the mucosa and in the fibrous tissue around the cartilage, especially at the bronchial bifurcations. Involvement of these foci of lymphoid tissue probably accounts in large measure for the formation of the endobronchial plaques and ulcerations. In these cases granulomatous bronchitis may be extensive, justifying the term panbronchitis. Plaques of granulomatous tissue project into the bronchial lumen and may become superficially ulcerated. In only one of these cases was the intrabronchial spread the predominant lesion. In all the others an associated diffuse peribronchitis or massive lobar type was superimposed as the main type of parenchymal spread.

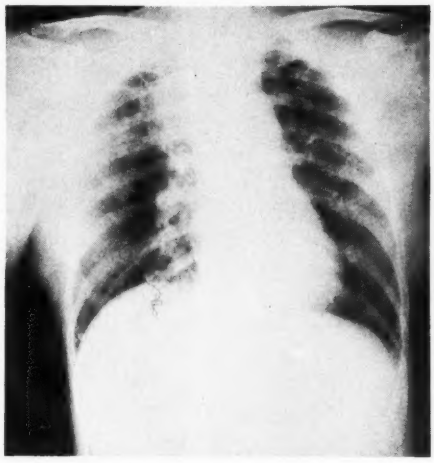

Fig. 3. Mediastinal, hilar, infiltrative parenchymal, and miliary Hodgkin's disease, verified by autopsy.

Miliary foci of Hodgkin's disease within the parenchyma occurred in 4 of our cases. Versé believes that these foci represent a lymphohematogenous spread of the lesions. In one of our cases this type of distribution was suggested by the x-ray study and was verified postmortem (Fig. 3). In all 4 cases other types of parenchymal spread were also evident; one showed several confluent lobular or nodular areas of distribution; the other three showed areas of diffuse peribronchial or lobar infiltration plus the multiple miliary foci found at quite a distance from the predominant areas of lung involvement. These minute foci resemble the tubercles of miliary tuberculosis. Their formation probably occurs in the same way, *e.g.*, spread of the causative agent with subsequent tissue reaction at the sites of localization of the etiologic factor.

Moolten reported an autopsied case hav-

ing a massive polypoid endobronchial mass which caused atelectasis. In one of our cases a positive biopsy from an ulcerated plaque in the right main bronchus at bronchoscopy led to the diagnosis of Hodgkin's disease. Hurd (20) in 1922 reported such a case, in which bronchoscopic biopsy had been obtained from a lesion causing bronchial stenosis. In rare types of Hodgkin's disease in which the disease within the lung is predominantly intrabronchial, this lesion might lead to stricture of the bronchial lumen with consequent atelectasis. In such a unique case a differential diagnosis between Hodgkin's disease and bronchogenic carcinoma would be impossible without bronchoscopic biopsy. Fortunately these cases are rare, and atelectasis as a result of endobronchial stricture by Hodgkin's disease is infrequent. Atelectasis in Hodgkin's disease, when it occurs, appears usually to be a late effect, caused by bronchial occlusion by invasion from without or by pressure from a massive pleural exudate. In 2 of our cases large tracheal ulcers of specific tissue were found, one of which became transformed into a tracheo-esophageal fistula.

The formation of fistulae by lymphogranulomatous destruction of tissue has been observed by several authors. Radauskas (43) called attention to the development of bronchial fistulae in Hodgkin's disease but did not specify what other structures were involved.

In one of our patients, a woman thirty-four years of age with generalized Hodgkin's disease, a tracheo-esophageal fistula resulted from extension of a tracheal ulcer into the esophagus. This fistula was suggested by roentgenography six months before the patient's death, when barium was found in the pulmonary tract after barium swallowing (Fig. 4). Bilateral lung abscesses subsequently developed, one in the middle lobe of the right lung, 5 cm. in diameter, the other in the left lower lobe, 2.5 cm. in diameter. At autopsy the point of fistula formation was found 5 cm. above the bifurcation of the trachea. The communication was 2 mm. in diameter and was lined by granulomatous tissue especially noticeable around its tracheal orifice. The bilateral lung abscesses were lined by specific Hodgkin's granulomatous tissue plus non-specific granulation tissue. Abscess cavities located between the posterior surface of the middle lobe of the right lung and the parietal pleura contained no pus, as the abscess had apparently drained into one of the larger bronchi. Massive involvement of both lungs with Hodgkin's tissue was also present (Fig. 5).

Weber (59) in 1930 and Pesonen (40) in 1938 have previously reported tracheo-esophageal fistulae. In Pesonen's case the fistula was demonstrated with lipiodol and verified at autopsy.

Other fistulae we have observed involved the esophagus primarily. In one case a 5-mm. opening into the esophagus located at the junction of its lower and middle thirds communicated with a necrotic cavity within an enlarged posterior mediastinal node that had ruptured. The fistula, then, resulted from necrosis of an enlarged node which later extended into the adherent esophageal wall. This patient also had a cavity in the left upper lobe containing necrotic material. This cavity communicated with enlarged pretracheal nodes. Two other cavities, measuring up to 3 cm. in diameter, probably resulting from necrosis of the specific Hodgkin's tissue, were found in the right lung. Kottler (25) in 1930 reported a case almost similar in pathological findings.

In another case a large defect was found in the esophageal wall just below the tracheal bifurcation. This defect led to the formation of a large posterior mediastinal abscess which extended into the adherent left lower lobe, causing marked necrosis of the lung parenchyma forming one wall of the abscess cavity. The other case with fistula formation in the esophagus has been mentioned above as a part of a tracheo-esophageal fistula.

Cavitation of the lung due to Hodgkin's disease is an infrequent feature. Bouslog and Wasson (3) reported a case in 1932. At necropsy the walls of the cavity were

Fig. 4. Roentgenogram believed to show tracheo-esophageal fistula in Hodgkin's disease. At autopsy a fistulous tract was found in the trachea about 5 cm. above the bifurcation, communicating with the esophagus.

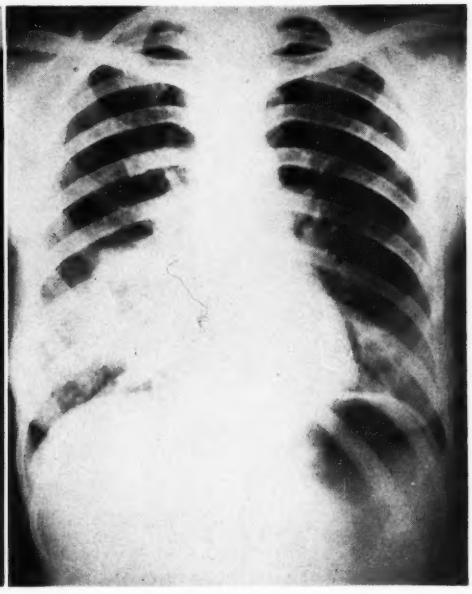

Fig. 5. Abscess cavity in right lung resulting from tracheo-esophageal fistula. At necropsy the wall of the cavity was found to contain specific Hodgkin's granuloma plus non-specific granulation tissue. Same case as Figure 4.

found to be composed of lymphogranulomatous tissue. These writers reported their case as the first in which cavitation was found in Hodgkin's disease. As a matter of fact, Claus (4) as early as 1888 had reported a case of cavitation occurring in Hodgkin's disease. Yamasaki (4) in 1904 described multiple small cavities formed by fusion of caseating nodules in his case. Dvorak (9) in 1927 reported a case with a large cavity in the right lung. The patient had died because of rupture of the left common carotid artery into the esophagus. Weber (59) in 1930 reported probably the largest cavity found to date. A cavity the size of a "child's head" in the right upper lobe communicated through a 2-cm. orifice with another cavity the size of a fist in the right lower lobe. Weber believed the cavities resulted from a combination of irradiation and mixed infection. There was no evidence of tuberculosis. Lenk (29), Pierce, Foulon, Lubarsch (4) and Altman (29) are among others who have reported cases with cavitation of the lung showing no unusual features. Hardin (18) in 1939 published a case with massive atelectasis of the right lung caused by intermittent occlusion of the bronchi by a tenacious mucopurulent exudate arising from a severe bronchitis secondary to direct involvement of the bronchi with Hodgkin's disease. Multiple cavities occurred in the lung secondary to the atelectasis. The cavities were lined in most instances with specific Hodgkin's tissue. At no time had the lung been exposed to irradiation.

Radauskas in 1936 reported a case with a cavity the size of a "man's fist" in the left lung, which was operated on and drained as a lung abscess. The patient had previously been treated as suffering from tuberculosis with cavity formation. Rarely a cavity may perforate and give rise to a pyopneumothorax or empyema (17, 25).

Sternberg (29) reported a case with cavitation. The cavity wall was lined with both Hodgkin's and tuberculous tissue.

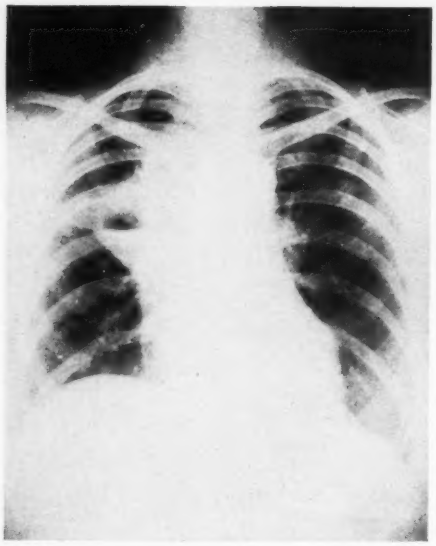

Fig. 6. Cavitation of the lung in Hodgkin's disease. Diagnosis was made by bronchoscopic biopsy of a granulomatous ulcer in the right main bronchus.

One may readily see from the above reports how cavitation may lead to an erroneous diagnosis of tuberculosis, lung abscess, or congenital lung cyst.

In our own material we have observed 3 cases with cavitation. In one case there were multiple cavities measuring up to 4 cm. in diameter scattered throughout both lung fields. This patient also developed an esophageal fistula connecting with an enlarged centrally necrosed posterior mediastinal node. The second patient with cavitation had massive infiltration of both lungs with Hodgkin's tissue. A lung abscess cavity measuring 5 cm. in diameter resulted from a tracheo-esophageal fistula. The wall of this cavity in the right middle lobe was composed of non-specific plus specific Hodgkin's granulation tissue. Another abscess cavity 2.5 cm. in diameter was found in the left lower lobe. This case cannot be taken as a true case showing cavitation because of the superimposed secondary infection resulting from the fistula.

In our third case, a large cavity, $5 \times 6 \times 7$ cm., was found in the right upper lobe. The cavity was well drained by the main bronchi to this lobe and because of this drainage, the greater part was not filled with purulent material. The wall of the cavity was lined by Hodgkin's granulomatous tissue as verified by microscopic examination. A diagnosis of Hodgkin's disease in this case had been confirmed by bronchoscopy biopsy from a granulomatous ulcer in the right main bronchus (Fig. 6).

Cavitation may occur spontaneously, as is shown in the first of the three cases just described. This breaking down of tissue probably resulted from necrosis of the nodular lesions within the parenchyma due to obliteration of the blood supply to the central portions of the lesion. The same result may occur after irradiation of these lesions, probably because of impairment of the blood supply leading to necrosis. In Hardin's case with cavitation, however, no irradiation had been given over the areas wherein cavitation occurred. The process of central necrosis may thus occur spontaneously, without irradiation or secondary infection, in a process analogous to that which occasionally occurs in lymph nodes affected by Hodgkin's disease. We have observed several cases in which the nodes broke down without previous irradiation. Culture of the necrotic material obtained by aspiration yielded no bacterial growth.

Other miscellaneous findings which we have observed in our series were a combination of actinomycosis and Hodgkin's disease in one case, active tuberculosis and Hodgkin's disease in the parenchyma in 4 cases, and development of a terminal monocytic leukemia in one case. The mixed lesions always give rise to some speculation concerning etiological or pathological relationship. Some authors (11, 30) believe Hodgkin's disease and tuberculosis are closely related as to etiology. Moolten develops an analogy between the lesions of Hodgkin's and actinomycosis as proof of a hypothetical virus as causing Hodgkin's disease and stresses the similarity of pathological lesions in tuberculosis, Hodgkin's, and actinomycosis as proof that Hodgkin's

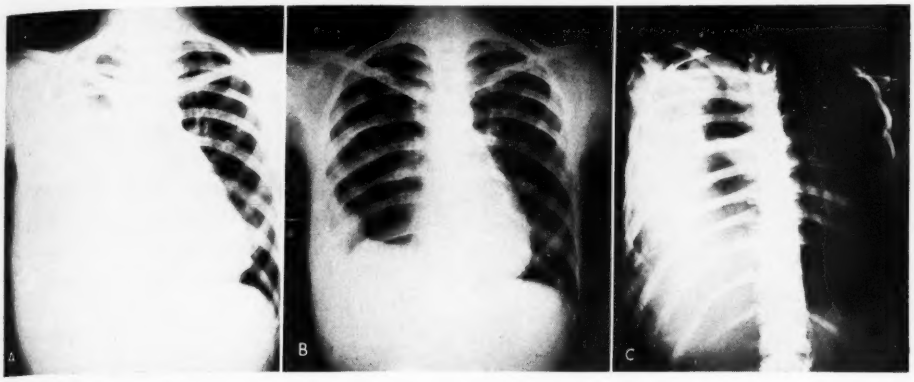

Fig. 7. Hodgkin's disease. A. Large intrathoracic mass. B. Residue of mass on lateral chest wall after irradiation. C. Spot film showing destruction of ribs. The mass probably originated in the pleura and secondarily invaded the ribs or *vice versa*.

disease is an inflammatory condition rather than a neoplasm. From an extensive study, most authors agree that lymphogranuloma is essentially a process of productive inflammation with particular activity shown by the reticulo-endothelial elements. Studies by Medlar (35, 36, 37), who promulgates a neoplastic etiology on the basis of a neoplasia particularly affecting the megakaryocyte of the bone marrow, need further verification by other students of this disease before this concept can be accepted. The weight of opinion shared by Ewing and others makes us strongly lean to the concept of Hodgkin's disease as primarily inflammatory. The disease may be regarded as one not necessarily primary in the lymphoid tissue, but as an affection of the mesenchymal tissues throughout the body. It is not within the scope of this paper to deal with such controversial issues (7, 16, 27, 31, 32, 38, 39, 47, 48, 57, 58).

TABLE III: AUTOPSY FINDINGS IN HODGKIN'S DISEASE

Authors	No. Cases	Mediastinal and/or Hilar Nodes (per cent)	Involvement of Parenchyma of Lung (per cent)	Pleural Involvement (per cent)	No Lesions in Chest (per cent)
Falconer and Leonard (7 authors)	125	...	37	..	..
Krueger and Meyer	16	100	50	..	..
Whitaker	7	85	28	..	..
Moolten	18	...	50	..	..
Craver and Vieta*	51	74	47	29	12

* Miscellaneous findings: Tracheal ulcers, 2 cases; tracheal esophageal fistula, 1 case; esophageal ulcerations or necrosis, 3 cases; bronchoscopic biopsy, 1 case; cavitation of the lung, 3 cases; actinomycosis and Hodgkin's, 1 case; tuberculosis in lung and Hodgkin's, 4 cases; terminal leukemia, 1 case.

In our 51 autopsied cases we have divided the intrathoracic manifestations into three main groups (Table III): mediastinal and/or enlargement of the hilar nodes 74 per cent; parenchymal involvement 47 per cent; parietal pleural involvement 29 per cent.

We call special attention to the high percentage of involvement of the parietal pleura (29 per cent). Characteristic lesions involving the pleural membranes may be divided into the following subgroups: (*a*) miliary, (*b*) scattered nodular or flat infiltrating, (*c*) massive elevated nodular, (*d*) chronic indurated forms as extensions from the ribs or lungs. The great majority of pleural lesions fall within the second of these groups.

Several cases were seen in which massive pulmonary involvement caused tough adhesions of granulomatous tissue to bind portions of the lung solidly against the chest wall. In some of these cases the process extended into the contiguous ribs. Involvement of ribs is not infrequent, and in some cases it was impossible to determine whether the Hodgkin's process in-

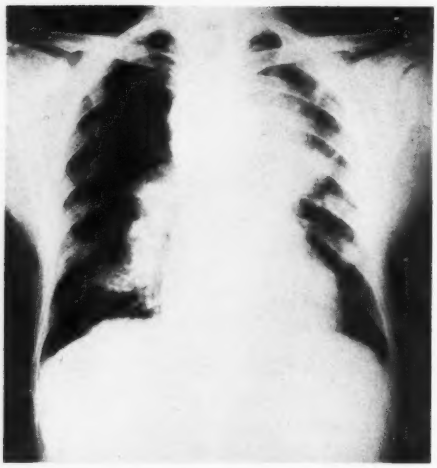

Fig. 8. Mediastinal, hilar, and parenchymal disease in lymphosarcoma. This film is representative of all the lymphomatoid diseases.

vaded the lung and extended transpleurally into the rib or whether the process began in the rib and secondarily involved the lung (Fig. 7). These lesions in combination were always of massive proportions.

In several cases the involvement of the diaphragmatic pleura was extensive. From these foci infiltrations extended through the diaphragm to invade the liver extensively and formed large areas of granulomatous tissue causing massive destruction of liver parenchyma. In life the clinical phenomena noted were hepatomegaly, long continued fever, and jaundice due to hepatic insufficiency.

The incidence of pleural involvement partly explains the frequency of large collections of pleural exudate found roentgenographically during life when other factors, as pressure on mediastinal veins due to mediastinal adenopathies, are not demonstrable. Pleural lesions may also be the factor characteristically causing the exudate to reform rapidly and persistently after repeated thoracenteses. The cytology of the fluid in some cases is purely lymphocytic, or it may be eosinophilic, with high fibrin content; analyses of the exudate may show it to be serosanguineous, serofibrinous, or chylous (5, 14, 45).

We have observed no case in which Hodgkin's disease was primary in the pleura. Several French authors (14) have intimated that the pleura may be the primary site of origin of this disease. To incriminate the pleura when other avenues of dissemination are more likely to be affected appears to be unwarranted theorizing.

In this discussion we have tried to correlate the known features of Hodgkin's disease and especially to stress the frequency of intrathoracic lesions, as encountered roentgenographically and at necropsy. In our small series—51 autopsied cases—a statistical analysis regarding all types shows that 88 per cent of cases examined at necropsy had some form of lesion caused by Hodgkin's disease within the thorax. The discrepancy in incidence between lesions found at autopsy and lesions shown by roentgenography indicates that more frequent x-ray examination of the chest could considerably raise the percentage of cases in which lesions are found while the patient is under treatment. The demonstrated vagaries in form and extent of the lesions of Hodgkin's disease within the chest lead to the conclusion that the roentgen picture of intrathoracic Hodgkin's disease is characterized by its variability, and the pathological lesions by their versatility.

LYMPHOSARCOMA

Under the classification of lymphosarcoma, we have included reticulum-cell lymphosarcoma, malignant lymphocytoma, and giant follicular lymphadenopathy (Brill-Symmers) (1, 44, 50). Cases in which the latter diagnosis was made have in several instances become transformed into reticulum-cell lymphosarcoma before death. Autopsy of these cases revealed lesions indistinguishable in extent or histology from those of patients who had classical histological lesions of lymphosarcoma.

In lymphosarcoma the roentgenographic features are not unlike those seen in Hodgkin's disease (Fig. 8). Only very limited sources were found in the literature with which we could compare our statistical re-

TABLE IV: ROENTGEN FINDINGS IN LYMPHATIC LEUKEMIA, LYMPHOSARCOMA, AND MYELOGENOUS LEUKEMIA

Authors	No. of Cases	Mediastinum	Infiltration	Isolated Nodules	Discrete Nodes at Roots	Pleural Thickening	Fluid
LYMPHATIC LEUKEMIA							
Kirklin and Hefke	48	21%	21%*				0%
Falconer and Leonard	30		30%*				
Craver and Vieta	158	36%	24.6%	1.9%	27%	12%	12%
LYMPHOSARCOMA							
Kirklin and Hefke	84	20%	20%*				
Falconer and Leonard	25		36%*				41%
Cutler	30	56%					
Craver and Vieta	239	26.7%	23.8%	5.8%	11.1%	9.6%	16.6%
MYELOGENOUS LEUKEMIA							
Craver and Vieta	52	0	7.6%	0	9.6%	1.9%	3.8%

* Calculations by Falconer and Leonard.

sults. Comparative case reports (6, 13, 24) show a tendency to base their figures on cases having only positive roentgenographic features instead of considering the total number of cases studied. In our series of 239 cases we have used Wessler and Greene's classification of topography. In comparing our cases with Hodgkin's disease, for instance, we find that the various lesions are seen less frequently, but the similarity in types is quite evident. Like other authors, we feel that there is no characteristic roentgen picture of intrathoracic lymphosarcoma, and in view of the morbid anatomy this conclusion is warranted.

In our series of 239 cases, as shown in Table IV, infiltration in the lung occurred in 23.8 per cent. Isolated nodular masses occurred in 5.8 per cent. The mediastinum was widened in 26.7 per cent, and discrete nodes at the lung roots were present in 11 per cent. Displacement of intrathoracic structures was found to be very rare even when mediastinal or hilar masses were of large size. This is a characteristic observation in all the lymphomatoid diseases and has been verified by other writers (24, 29, 49). Pleural effusion occurred in 16.6 per cent. Pleural thickening was demonstrable in 9.6 per cent.

The parenchymal infiltrations as shown in the x-ray film were usually diffuse. In many instances the infiltration appeared to affect the greater portion of a lobe of the lung by direct extension from the hilar structures. The formation of discrete lobular foci—5.8 per cent—nearly always accompanied the infiltrative lesions. In reviewing the postmortem material, however, one forms the impression that the most frequent type of lung lesion is circumscribed foci. Comparison between the cases reviewed roentgenologically (239) and the autopsied series (55 cases) does not permit any conclusion. Then, again, many of the cases autopsied had had irradiation therapy, producing regression of the infiltrative lesions. In our experience the infiltrative lesions have been more radiosensitive than the lobular foci, and this may account for the more frequent incidence of the circumscribed foci at autopsy, after irradiation to the lung lesions has been given.

Pulmonary involvement or pleural manifestations usually occurred rather late in the course of the disease, but despite this many cases were seen in which striking improvement in the patient's general condition followed irradiation of the affected areas. Thus, when parenchymal involvement is found, x-ray therapy should be used to its full limit. In some cases there was complete regression as disclosed by roentgen examination. Thus the induction of remissions by radiation therapy when the lung is involved is by no means hopeless. Treatment may prolong life for many months. We have observed this frequently enough to attempt treatment in almost all cases, despite widespread lesions. One cannot judge the radiosensitivity of the

disease within the lung until trial therapy is instituted.

In a postmortem analysis, again using the classification of modes of spread within the chest as advanced by Versé, we have found, like others, frequent enlargement of the mediastino-bronchial nodes, 64.7 per cent in this series of 55 cases (Table V). Cutler (6) in a series of 13 cases found these areas affected in 69 per cent. Symmers (49) in analyzing 17 cases was impressed by the massive involvement of the various structures within the thorax before any clinical symptoms were elicited. We, too, have seen that when lymphosarcoma invades the intrathoracic structures the involvement is widespread with the formation of large masses of neoplastic tissue.

Symmers (49), Cutler (6), and Falconer and Leonard (13) have all noted the considerable incidence of involvement of the pleura by large masses of tumor tissue. Our autopsied material shows this to be a striking feature in lymphosarcoma, 30 per cent of our cases showing extensive infiltration of the parietal pleura.

TABLE V.: AUTOPSY FINDINGS IN LYMPHOSARCOMA

Authors	No. Cases	Mediastinal and Hilar Nodes (per cent)	Involvement of Parenchyma of Lung (per cent)	Pleural Involvement (per cent)	No Lesions in Chest (per cent)
		(Thymus)		(Parietal and Visceral)	
Symmers	17	41		35	
				(Parietal)	
Cutler	13	69	23	54	
Falconer and				(Parietal)	
Leonard	8	87	87	62.5	
Craver and				(Parietal)	
Vieta	55	64.7	24.5	30	27

Table V summarizes our postmortem findings in the chest.

We have never seen in lymphosarcoma the formation of cavities or production of intrabronchial plaques or ulcerations (Table VII), which are striking features in the pathology of any series of Hodgkin's disease studied at necropsy. The commonest type of lymphosarcomatous involvement of the parenchyma takes the form of a more or less lobar (or diffuse) infiltration or the formation of confluent lobular or isolated circumscribed foci of neoplastic tissue. These isolated circumscribed foci probably represent true metastases in the great majority of cases. Invasion of intrapulmonic lymphoid follicles by the neoplasm may, however, be seen. In some instances a condensed peripheral rim of neoplastic tissue, probably the infiltrated capsule of a pre-existing node, is preserved; in others the "capsule" has been obliterated and invasion of the parenchyma from the nodal focus occurs, as a massive infiltrating process which may destroy an entire lobe of the lung. The incidence of parenchymal lesions as shown by roentgenography (23.8 per cent) agrees with the findings at necropsy (24.5 per cent). The number of cases analyzed in each group does not, however, warrant any conclusions on these percentage figures.

Observation of lesions extending from the lung through the pleura and diaphragm to affect large portions of the dome of the liver is not unusual. Retraction of the lung or displacement of the trachea so commonly seen in cases of carcinoma of the lung is rarely seen in lymphosarcoma despite various degrees of diffuse permeation of the lung parenchyma and the large masses found in the mediastinum.

Infiltration of the parietal pleura accompanies the other intrathoracic lesions. Frequently in this group (30 per cent at autopsy) the foci within the pleura were either large flat plaques or raised nodules of homogeneous neoplastic tissue. Miliary dissemination was not seen. On roentgenography pleural thickening was observed in 9.6 per cent of the series and pleural effusion in 16.6 per cent. In correlating the necropsy incidence of parietal pleural lesions (30 per cent) with those found roentgenographically, it is readily seen that the pleural lesions must be an important factor in causing the accumulation of pleural fluid during life. This is especially true when mediastinal or hilar adenop-

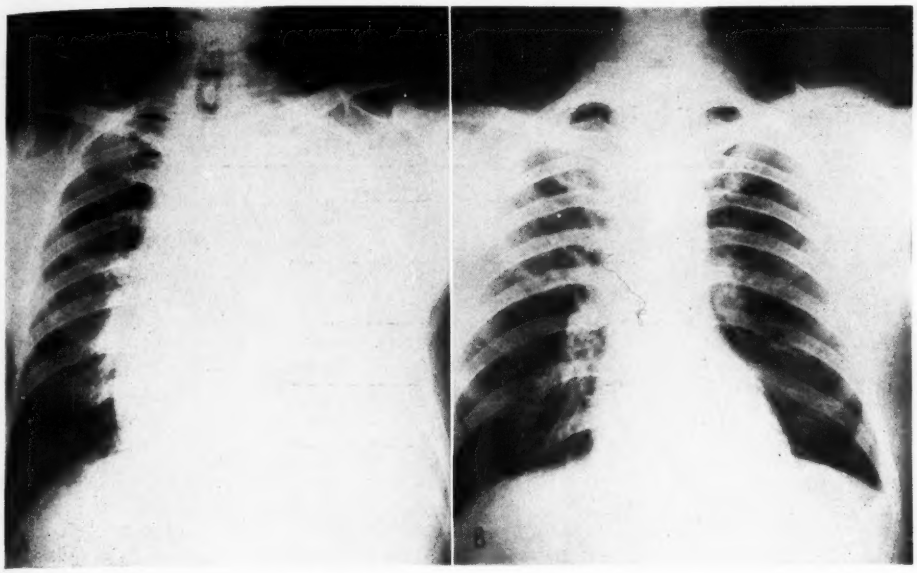

Fig. 9. Lymphosarcoma. A. Massive pleural effusion. B. Regression of exudate two and a half months after irradiation therapy. Thoracentesis was not done.

athies sufficiently large to cause venous blockage are not demonstrable by roentgen examination.

Irradiation of the chest in the presence of massive pleural effusion has caused disappearance of the fluid in many cases without resort to thoracentesis (Fig. 9). This therapeutic effect is partially explainable by the effect of the irradiation given to the lymphosarcomatous pleural lesions.

In the 239 cases analyzed by roentgenography, no instance of fistula formation was found involving trachea, esophagus, or bronchi. This feature is in contrast to Hodgkin's disease, in which fistula formation affecting these structures is not infrequent. In reviewing the literature we have found no example of this complication. Symmers (49) reported a case in which lymphosarcomatous tissue had invaded the right auricle of the heart producing a mushroom growth within the chamber. An explanation for the absence of fistula formation may be that lymphosarcomatous tissue is invariably proliferative, while in Hodgkin's disease, according to Moolten, the agent has proliferative and lytic plus toxic qualities of an inflammatory nature which readily cause the lesion to permeate walls of arteries or bronchi. By this hypothesis one can explain the necrosis of tissue in Hodgkin's disease leading to fistula formation or cavitation.

In this series of cases of lymphosarcoma the incidence of intrathoracic lesions is strikingly high, which is to be expected, as lymphosarcoma is a lymphatic system disease. Whether the process of spread into the lymphoid structures of the thorax is primarily hematogenous or lymphatic cannot be definitely stated at present. The free connection between the two systems of circulation through the thoracic duct may explain the widespread and often explosive dissemination of the disease process after a somewhat more localized primary involvement (10, 11). To date we have not seen an example of primary lymphosarcoma in the lung proper. It is our belief that the parenchymal and pleural involvements so frequently found are secondary foci, occurring probably in the main as a result of extension by cell embolism, either directly by way of the blood or by a retro-

TABLE VI: INTRATHORACIC LESIONS AS SHOWN BY ROENTGENOGRAPHY IN THE LYMPHOMATOID DISEASES (MEMORIAL HOSPITAL SERIES)

Diseases	No. of Cases	Mediastinum (per cent)	Discrete Nodes at Roots of Lung (per cent)		Infiltration (per cent)	Isolated Nodules (per cent)		Pleural Thickening (per cent)	Fluid (per cent)	No Evidence of Disease (per cent)
Hodgkin's disease	335	47.4	23.8			5.3		7.4	15.8	25.3
			58.5			38.5				
Lymphosarcoma	239	26.7	11.2			5.8		9.6	16.6	46.4
			33			23.8				
Lymphatic leukemia	158	36	27			1.9		12	12	28.4
			52			24.6				
Myelogenous leukemia	52	0	9.6			0		1.9	3.8	82
			9.6			7.6				
Mycosis fungoides	10	10	0			0		10	10	70
			10			30				
TOTAL CASES	794									

TABLE VII: POSTMORTEM FINDINGS CLASSIFIED BY THE METHOD OF VERSÉ (MEMORIAL HOSPITAL SERIES)

	Mediastinal Nodes	Hilar Nodes	I		II		III	IV		Parietal Pleural Nodules	Pleural Fluid	No Evidence of Disease
			By Hilum	By Medial Surface of Lung	Peri	Intra			V			
Hodgkin's disease 51	30	20	3	3	5	7	11	16	4	15	20	6
Lymphosarcoma and Brill-Symmer's disease 55	31	14	3	1	1	0	5	10 Sub-Pleural	2	17	21	15
Lymphatic leukemia 31	23	11	0	0	1	1	3 (1 lt. lung gangrene)	1 Sub-Pleural	1	2	9	5
Myelogenous leukemia 23	8	3	0	0	0	0	0	0	3	0	2	12

I. Mediastinobronchial node lesions with direct invasion of the lung.
II. Mediastinobronchial node lesions with peribronchial and intrabronchial spread.
III. More or less lobar (diffuse) infiltration of the lung with varying degrees of involvement of the bronchomediastinal nodes.
IV. Confluent lobular (isolated circumscribed) focal formations with involvement in varying degrees of the bronchomediastinal nodes.
V. Miliary (lymphohematogenous) foci with involvement in varying degrees of the bronchomediastinal nodes.

grade route through the lymph channels blocked by the primary nodal lesions. Spread by cell embolism or metastasis appears to be a more likely explanation for the origin of many of the extra-nodal manifestations of lymphosarcoma than development of the lesions *in situ* in pre-existing lymphoid tissue as a result of an etiologic agent causing a general neoplastic reaction in the lymphoid tissues as a whole.

LYMPHATIC LEUKEMIA

We have grouped our cases of pseudoleukemia, lymphatic leukemia, and lymphatic leukosarcoma under one classification, lymphatic leukemia.

In our roentgenographic analysis we are impressed by the frequency of the parenchymal infiltrations in the lung. This point has also been made by Kirklin (24)

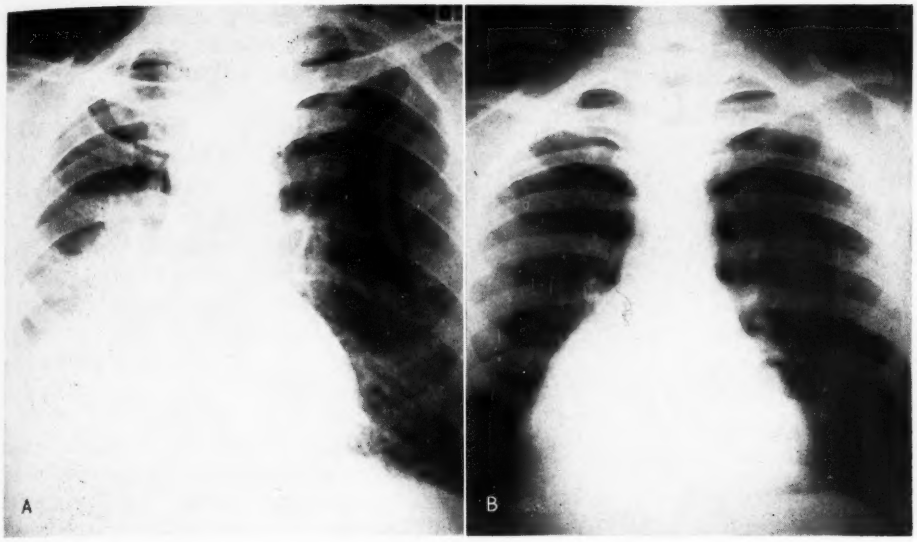

Fig. 10. Lymphatic leukemia. A. Massive lobar infiltration. B. Rapid regression of leukemic infiltration eleven days after irradiation therapy.

and Falconer (13). Involvement of the mediastinal and hilar nodes is the most frequent type (Fig. 8), but, as has been shown at autopsy, these nodes may be of such dimensions that they are not demonstrable roentgenographically. In our comparative study of 158 cases we have placed the various types of lesions in the usual groups. It should be mentioned that usually different types of lesions occur together. In statistical analyses by Falconer and Leonard, and Kirklin and Hefke, the percentage of cases given as showing pulmonary involvement includes enlargements or involvement of bronchial and hilar lymph nodes, pleura, and the parenchyma of the lung. There is, therefore, some discrepancy in the comparison in Table IV, but this is not marked when one considers the number of cases compared and the various subgroupings of the intrathoracic lesions. One can see the frequent parenchymal involvement as shown by the roentgen film (Fig. 10).

Isolated nodules of leukemic tissue within the parenchyma, in our experience, are rare phenomena in the lymphatic leukemias (Fig. 11). Lenk (29) calls attention to the fact that an isolated parenchymal nodule of leukemic tissue may disappear following irradiation of a part of the body far removed from the lung. He does not believe this ever happens in cases of lymphosarcoma or Hodgkin's disease. We have recently seen it occur in a case of lymphatic leukemia now under observation. Irradiation of a group of enlarged inguinal nodes was followed by the disappearance of a sharply circumscribed focus, undoubtedly metastatic, measuring 2 cm. in diameter, in the periphery of the lung. This observation may be of value in the differential diagnosis of the aleukemic types of leukemia when the blood picture is not diagnostic or when enlarged nodes are not available for biopsy.

Comparative autopsy results from other authors are not available. In our own series we have grouped the lesions according to Versé's classification and have found that the most common focus is an enlargement of the mediastinal or hilar nodes. We did not observe any case in which the lung parenchyma was extensively invaded through the hilus or medial surface of the lung by a transpleural spread. The most common type of parenchymal involvement

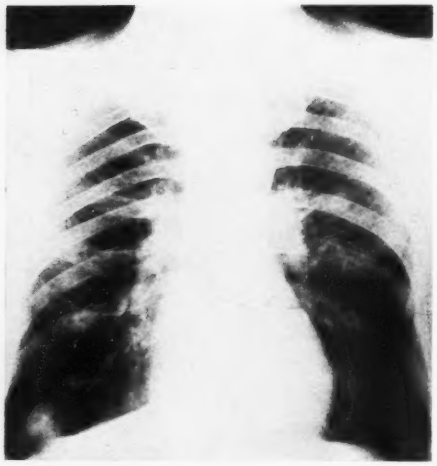

Fig. 11. Solitary nodule of lymphatic leukemic tissue in right lower lobe. This is a rare finding in our observations.

we have seen is either a more or less lobar infiltration or the formation of large confluent foci of leukemic tissue, making it almost impossible to classify the type of spread of leukemic tissue into the lung (Fig. 10). The predominant spread appeared to be peribronchial, however, following the interstitial tissue planes, where lymphoid tissue is present normally. One case showed gangrene of the left lung caused by a breaking down of massive leukemic deposits by a secondary infectious process. One case showed the formation of intrabronchial plaques of leukemic tissue. Miliary pulmonary infiltration by lymphatic leukemia and nodules of lymphatic leukemia in the parietal pleura are rare. Miliary disseminations were seen in only one case. The parietal pleura was extensively involved in only two cases. In comparison with analogous lesions in Hodgkin's disease and lymphosarcoma, the pleural manifestations of lymphatic leukemia as shown by roentgen examination and autopsy are quite similar. It must be noted that cases showing terminal pneumonia with a leukemic infiltration as the cellular reaction to the pneumonic process cannot be considered as presenting true types of leukemic parenchymal infiltration.

In our series there is fairly close agreement in incidence of parenchymal lesions of lymphatic leukemia as shown roentgenologically (24 per cent) and at autopsy (19 per cent).

MYELOGENOUS LEUKEMIA

We have found few references to myelogenous leukemic manifestations within the chest, in the current literature. Von Domarus (56) in a review of the literature noted that mediastinal tumors are rarely found in this disease. Sporadic case reports tell of varying degrees of parenchymal involvement first noticed on roentgen examination and confirmed at autopsy. Joachim and Loewe (22) reported a case with a peculiar pneumonic process which at autopsy showed many nodular masses in the parenchyma, apparently the result of repeated infarctions secondary to vascular occlusions with myeloid cells and subsequent infiltration of the infarct with myeloid tissue.

In our own roentgenographic material we found no instance of mediastinal tumor. Discrete nodes at the lung roots occurred, however, in 9.6 per cent of the cases. Parenchymal involvement as shown by peripheral infiltration was present in 7 per cent of this small series of 52 cases (Table IV). Peribronchial and hilar thickenings difficult to interpret are not included in the incidence of intrathoracic lesions in any of our tables.

In our 23 autopsied cases (Table VII) we found myeloidization of the grossly enlarged hilar or mediastinal nodes in 47 per cent. In other words, enlarged nodes, which seldom measure above 3 cm. in diameter in these areas, when sectioned and studied microscopically, showed myeloid infiltration in 47 per cent of autopsied cases of myelogenous leukemia. Parenchymal infiltrations usually occur as miliary foci of myeloid tissue; this feature was observed in 3 cases or 13 per cent of our series.

The formation of large foci or marked infiltration was not observed in any case, nor was there any example of parietal pleural involvement. We believe, however, that

in cases of myelogenous leukemia where the process approaches the myeloid sarcomatous type we should find more frequent evidence of myeloid infiltration of the intrathoracic tissues (Table VIII).

TABLE VIII: AUTOPSY FINDINGS (MEMORIAL HOSPITAL SERIES)

Diseases	No. of Cases	Mediastinum and/or Hilar Nodes (per cent)	Involvement of Parenchyma of Lung (per cent)	Involvement of Parietal Pleura (per cent)	No Lesions in Chest (per cent)
Hodgkin's disease	51	74	47	29	12
Lymphosarcoma	55	64.7	24.5	30	27
Lymphatic leukemia	31	83	19	6	16
Myelogenous leukemia	23	47 (myeloidization of nodes)	13	0	52
TOTAL	160				

We have no explanation for the infrequency of involvement of the intrathoracic structures in myelogenous leukemia. This is true also of other manifestations of the disease; bone lesions and skin involvement, for instance, are not as often demonstrated in myelogenous leukemia as in lymphatic leukemia. It may be that the explanation lies in the relative primary scarcity of myeloid tissue as compared to the wide-spread distribution of lymphoid tissue.

MYCOSIS FUNGOIDES

Mycosis fungoides, for lack of more precise knowledge, has been included in this series as a separate entity. Warthin (58) believes that in the great majority of cases the disease is manifested histologically as a small-cell lymphoblastoma involving the primitive lymph follicles of the papillary layer of the dermis which coalesce to form the fungoid tumors of the skin, the process becoming generalized at last in all of the lymphoid structures of the body. Aside from the skin involvement, which may precede or follow that of the regional nodes, the pathologic picture is that of a generalized lymphoblastoma. Thus we have seen cases in which the skin manifestations are those of a mycosis fungoides and the terminal picture is that of a lymphosarcoma or leukemia.

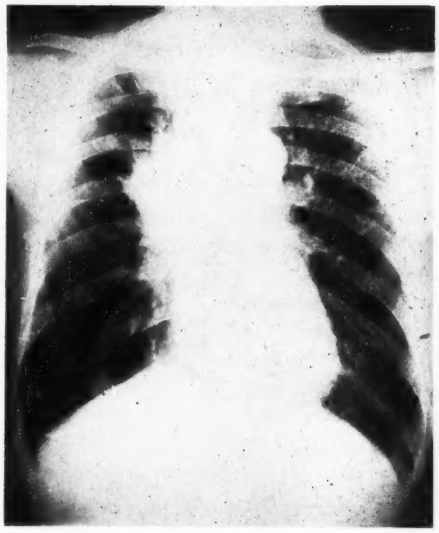

Fig. 12. Mediastinal and hilar masses plus parenchymal infiltration in a case of mycosis fungoides.

In analyzing 10 cases of mycosis fungoides roentgenographically (Table VI) we found that 10 per cent showed the formation of a mediastinal mass and 30 per cent a parenchymal lung infiltration similar to that seen in lymphosarcoma or leukemia but usually with more massive and distinct involvement demonstrable in the roentgenogram than in the usual cases of lymphatic leukemia (Fig. 12).

As none of these cases was autopsied we were unable to verify our conclusions in this report. We have one case, however, in which the skin nodules on biopsy showed a classical mycosis fungoides while at autopsy the lungs and lymph nodes showed infiltrations indistinguishable from those of lymphosarcoma.

SUMMARY

In a roentgenographic analysis of 335 cases of Hodgkin's disease, we have been able to demonstrate intrathoracic lesions

of one type or another in 74 per cent, the parenchyma being involved in 38.5 per cent, the pleura in 7.4 per cent and pleural exudate being seen in 15.8 per cent (Tables II and VI).

Postmortem we found demonstrable lesions within the thorax in 88 per cent of the cases. The mediastinum or hilar nodes or both showed disease in 74 per cent; the parenchyma was involved by various types of lesions in 47 per cent, and the parietal pleura in 29 per cent. In only 12 per cent of the autopsied cases of Hodgkin's disease was there an absence of any intrathoracic granulomatous or sarcomatous process (Tables III and VIII).

Of 239 cases of lymphosarcoma analyzed by roentgenography, 54 per cent showed some type of intrathoracic involvement; 24 per cent showed involvement of the lung either massively or in the form of diffuse infiltrations or discrete foci of neoplastic tissue; about 10 per cent showed a thickened pleura, and 16.6 per cent had a pleural effusion during the course of the disease (Tables IV and VI).

At autopsy in lymphosarcoma one may expect to find enlarged mediastinal and/or hilar nodes in 65 per cent; parenchymal lung lesions in 24.5 per cent; and involvement of the parietal pleura in 30 per cent. In 27 per cent of our cases we found no evidence of intrathoracic lymphosarcoma at autopsy. Thus intrathoracic lesions appear to be of less frequent occurence than in Hodgkin's disease (Tables V and VIII).

In 158 cases of lymphatic leukemia studied roentgenographically, all proved by biopsy or blood examination, intrathoracic involvement was found in 72 per cent. The majority of these lesions (52 per cent) are diagnosed as enlargement of hilar or mediastinal nodes or both, but the lung parenchyma was involved in 24.6 per cent; the pleura in 12 per cent; and pleural effusion was demonstrable in 12 per cent (Tables IV and VI).

In 31 cases coming to autopsy the mediastinal or hilar nodes or both showed evidence of lymphatic leukemia in 83 per cent; the parenchyma in 19 per cent; and the parietal pleura in 6 per cent. Altogether 84 per cent of our cases of lymphatic leukemia showed intrathoracic lesions, exclusive of the heart and pericardium, at necropsy (Tables VII and VIII).

Of 52 cases of myelogenous leukemia, 82 per cent showed no lesions roentgenographically. No mediastinal tumors were seen. Discrete nodes at the lung roots were seen in but 9.6 per cent and parenchymal infiltration in only 7.6 per cent. Pleural thickening and accumulation of fluid are rare, occurring in but 1.9 per cent and 3.8 per cent of the cases, respectively (Tables IV and VI).

In 23 autopsied cases of myelogenous leukemia, we found myeloidization of enlarged mediastinal or hilar nodes in 47 per cent; 13 per cent showed lesions in the lung parenchyma and in 52 per cent of the cases no chest lesions of any type were found (Tables VII and VIII).

In 10 cases of mycosis fungoides mediastinal or hilar nodes were demonstrable in 10 per cent and parenchymal infiltration in 30 per cent. We had no autopsy material in this disease as a basis for comparative study (Table VI).

Thus in a series of over 794 cases examined roentgenographically and in 160 cases studied postmortem, we have shown the frequency of the incidence of intrathoracic manifestations. In our own series we believe that roentgen films have not been taken frequently enough. This is especially true in the cases of myelogenous leukemia. We believe that if more roentgen examinations of the chest are made, the incidence of lesions within the chest will be even greater than appears from this series.

CONCLUSIONS

(1) Lesions of the lung in the lymphomatoid diseases are probably much more common than is generally known.

(2) There is no way of making diagnosis of these lesions, as their form is extremely variable.

(3) A note of warning must be sounded.

If a patient has a lymphomatoid disease, he may also have another type of tumor. Four malignant tumors of the gastro-intestinal tract were found in this series of 160 autopsied cases of lymphomatoid diseases. One was a carcinoma of the pancreas; three were carcinomas of the colon.

(4) Cavitation of the lung and the formation of broncho-esophageal fistulae may occur in Hodgkin's disease.

(5) The intrathoracic lesions may be rather silent clinically, producing negligible physical signs and symptoms. Therefore, only by more frequent roentgenograms of the chest can lesions be detected and the resulting knowledge be applied in the care of patients suffering from the lymphomatoid diseases.

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DISCUSSION ON MEDIASTINAL AND PULMONARY CHANGES IN ERYTHEMA NODOSUM AND INTRATHORACIC MANIFESTATIONS OF THE LYMPHOMATOID DISEASES

LeRoy Sante, M.D. (St. Louis, Mo.): The paper on erythema nodosum presents, in my opinion, a very commendable piece of research. Here we have a condition, the etiology of which is not known and concerning which there are many controversial points. With roentgen examination we have a method by which the inner structures of the body can be explored for manifestations of the disease and which may yield valuable information concerning its nature.

The authors have shown that in certain cases of erythema nodosum there is associated hilar or mediastinal node enlargement, which by presumption might be considered as an indication of a tuberculous nature of the condition I am sure, however, that I can show a number of erythema nodosum cases in which x-ray examination failed to disclose any hilum or mediastinal lymph node involvement. In fact, in only one of my cases was any enlargement of the hilum nodes found. If erythema nodosum were so constantly associated with tuberculous disease, we might reasonably expect to find a large number of cases in our tuberculosis sanatoria. On the contrary in Koch Hospital for tuberculosis in St. Louis only 7 cases were seen in fifteen years. In other words, I think there is still considerable question as to whether or not erythema nodosum represents a single disease entity; I am not sure that it doesn't have a number of causes, of which tuberculosis is only one This method of approach to the problem which has been presented is, however, very commendable, and should find greater use in clinical research problems of this type.

As to the paper on lymphosarcoma and lymphomatous diseases, I think we will all agree that this represents a monumental statistical study. To attempt an analysis of such tables and figures in a few minutes would fail to do the paper justice.

It seems to me the point which is definitely proved by the paper is that, since the various lymphomatous diseases produce similar appearing lesions in the chest, a differential diagnosis cannot be made from the chest film alone. There are predominant features in each particular disease, as shown by the charts: mediastinal enlargement, lymph node enlargment, isolated nodular involvement of the parenchyma of the lung, and finally pleural involvement; but any or all of these may occur in any of the lymphoblastomata. The blood findings, of course, differ, and these may establish the diagnosis. I think that the charts go even further, indicating the various types of invasion, the manner and location of the disease, and the complications that result, indicating thereby that the reactions produced by these various diseases in the living tissue are not the

same, and that these must, therefore, be different entities or at least different manifestations.

Only by the analysis of such large numbers of cases as were shown here today, and comparison with other similar studies made in the past, shall we come to any conclusion on these very interesting and very prevalent conditions—the lymphomatous diseases.

Howard P. Doub, M.D. (Detroit, Mich.): In the paper of Dr. Pohle and Dr. Paul the interesting features are the discussions of etiology and of differential diagnosis. The etiology would appear to have something of a geographical basis. In other words, if one studied European literature he would come to the conclusion that the disease is unquestionably tuberculous. If, however, cases reported from this country are taken into consideration, other factors are found to play a rôle, as was stated by Dr. Pohle. The etiological factor cannot always be proved.

Wallgren has expressed the view that erythema nodosum should be regarded as a non-specific, allergic cutaneous eruption which appears especially in tuberculosis but occasionally in other infections, or may even possibly be caused by a non-infectious agent. That, I think, is a very good statement.

In regard to the differential diagnosis, one must, of course, take into account all the diseases which were discussed in the second paper. Sarcoidosis may produce similar changes in the chest and they have been recorded also in coccidioidomycosis.

I looked over a few of our cases and discovered 12 with positive findings. Unfortunately I cannot tell the number of negative cases as I had not the time to go into all of them. Our results, however, were practically identical with those of Dr. Pohle.

Of the 12 cases, 4 could be classified as having very large hilar nodes, which could easily be mistaken for lymphosarcoma; 4 had what I call large mediastinal or hilar nodes; 3 had hilar nodes of moderate size, and 1 showed just a few changes which could be regarded as within the range of normal. Of these 12 patients, 4 had evidence of tuberculosis: 3 had calcified nodes in the chest and 1 had pleurisy with effusion.

The fine statistical paper presented by Dr. Vieta, as Dr. Sante says, cannot be thoroughly digested in a short time, but it is an excellent study to have in the literature for future reference. That the postmortem figures are so much higher than those obtained before death is due probably to two factors—one is that at the time of postmortem examination the lesions were further advanced; the other that the antemortem methods of examination are naturally less exact.

Our experience with these lesions roughly parallels the experience of Vieta and Craver. We have made no detailed statistical study such as theirs.

There is one type of case which, to me, has always been interesting and to which I called attention some time ago. This is a type which is usually diagnosed as lymphosarcoma. There is a large tumor in the mediastinum with a normal or practically normal blood count. After irradiation the tumor disappears, but at a later date the patient returns with a high lymphocytic count and all the typical findings of lymphatic leukemia.

There are two schools of thought regarding this change in the clinical picture. Some say that such a case is originally lymphosarcoma, but that when the process involves the bone marrow, the lymphosarcoma is converted into a lymphatic leukemia. Others believe that the case is originally one of lymphatic leukemia in an aleukemic stage. I subscribe to the view that the condition never was a sarcoma.

I have seen several such cases, and several others have been reported, especially by Dr. Evans and Dr. Leucutia.

Dr. Perry H. Shaw (Binghamton, N. Y.): I should like to ask Dr. Vieta if in closing he will say a few words about metastatic characteristics of Hodgkin's diseases. Was there evidence at autopsy of metastasis to the skull in any of these cases? I have a patient, now seventeen, in the fifteenth month of the disease, who has a sympathetic involvement of the third nerve on the left.

Ernst A. Pohle, M.D. (*closing*): I am very glad to learn that Dr. Doub's experience has been similar to ours and that apparently there are cases in other parts of the country of the same type that we have observed.

I hope that our paper did not give the impression that we thought that tuberculosis and erythema nodosum *must* necessarily go together. I am in full accord with Dr. Sante and do not question that there is still some doubt as to the tuberculous nature of erythema nodosum. The fact remains, however, that we found some evidence pointing in that direction and there is the definite fact that several cases responded readily to x-ray therapy.

The main reason for our presentation was to bring the subject to your attention and induce some of you to watch for these cases or perhaps search your records so that our knowledge of this undoubtedly interesting relationship may be increased.

John O. Vieta, M.D. (*closing*): I am sorry that Dr. Craver is not here to discuss this paper personally. In answer to the question asked by Dr. Shaw, I believe his patient must undoubtedly have involvement of the brain by Hodgkin's disease to account for the neurological findings. In many cases satisfactory regression of the lesions in the nervous system may be obtained by fairly intensive x-ray therapy. Affection of the nervous system in Hodgkin's disease is not unusual. In lymphosarcoma the disease not infrequently extends into the brain from the nasopharynx.

As I have said before, I believe that Hodgkin's disease may involve the mesenchymatous tissues of the body wherever found. The bones are probably involved in about 18 to 25 per cent of the cases.

Roentgen Therapy for Chronic Macrolymphocytic and Mesolymphocytic Lymphatic Leukemia[1]

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ROENTGEN THERAPY long has been an established method of treatment for all types of chronic leukemia. We are all well aware of the necessity of some caution in treating leukemia, whether of the myelogenous or the lymphatic type. We are aware, also, of the pitfalls encountered in treating the relatively acute and subacute types of the disease. Every radiologist realizes that leukemia may follow an erratic course during roentgen treatment; occasionally, too, for no apparent reason a poor result will be manifested. Our experience has been like that of others and our object in this paper is to describe a phase of lymphatic leukemia which deserves special consideration. We do not suggest that this is a new type of lymphatic leukemia, but we think it is vitally important that the therapeutic radiologist be aware of the difficulties encountered in treating this phase of the disease. We propose the title, "chronic macrolymphocytic and mesolymphocytic lymphatic leukemia," to describe the characteristic type of cell found on examination of the smear.

The clinical manifestations of this phase of leukemia are not unusual, in that adenopathy may be found in the cervical, axillary, and inguinal regions, as well as in the mediastinum and retroperitoneal area. In our series of cases it was not uncommon to find enlargement of the liver and spleen. The manifestations may be uniform or they may involve one or more of the regions listed; however, extensive involvement is usually present. The general condition of the patient is no different from that to be expected in any phase of lymphatic leukemia. The size of the involved nodes may vary considerably, but this is not an indication of the severity of the disease. Careful examination of blood smears by a competent hematologist will yield the only clue to the phase of leukemia. The age of the patient with this type of involvement varies, but in our series of cases the disease has been found most commonly among adults who have passed the fifth decade of life.

In reviewing the blood picture of patients with chronic lymphatic leukemia who exhibited great sensitivity to roentgen therapy, it was found that the large majority of lymphocytes were of macrolymphocytic or mesolymphocytic type in contrast to the usual predominance of microlymphocytes and mesolymphocytes. At first glance, the blood picture may be confused with that of acute leukemia, but detailed study of the morphology of these cells reveals that they are not lymphoblasts. The great majority of lymphocytes do not show much immaturity of the nucleus, but the latter is large and there is abundant cytoplasm. The nuclear chromatin is of the typical heavy block type seen in the practically mature or mature lymphocyte with abundant parachromatin, and distinction from very immature lymphocytes is readily made by this nuclear pattern. The cytoplasm is usually robin's egg blue, non-vacuolated and may or may not contain azurophilic granules. Approximately 5 per cent of cases of chronic lymphatic leukemia seen at the clinic are of the macrolymphocytic and mesolymphocytic type.

Treatment for this phase of leukemia must be carried on cautiously. The use of massive doses of roentgen rays is contra-

[1] Presented before the Twenty-sixth Annual Meeting of the Radiological Society of North America, Cleveland, Ohio, December 2 to 6, 1940.

indicated. In this phase of leukemia we have found that when doses of 300 to 500 roentgens are used, the leukocyte count changes radically; it can be reduced as much as 50 per cent in twenty-four hours. Although a rapidly decreasing leukocyte count is dangerous at any time in leukemia, the real danger in this phase of leukemia is not primarily only in the rapid reduction of the leukocyte count but in the effect on the chemical constituents in the blood. With a radical reduction in the leukocyte count we have found that the blood urea may increase markedly within a period of twenty-four to forty-eight hours. In a number of cases we have seen the concentration of urea in the blood double or triple. One explanation for this is the probable increase in the waste products from the destruction of the leukocytes and the inability of the renal system to handle the elimination of these products. A second and more likely explanation is the probable involvement of the kidneys themselves, especially about Bowman's capsules. In the last two years, because of the possibility of renal involvement, we have attempted to begin our course of treatment by giving applications to the posterior part of the abdomen and directing the rays to the renal region. It is our feeling that thus the involvement in Bowman's capsules is lessened and the elimination of the waste products is therefore considerably enhanced. During the treatment of this phase of leukemia we find it is as important to determine the concentration of urea in the blood daily as to make a daily leukocyte count.

Our course of treatment for this phase of leukemia consists of irradiation of the regions of involvement, giving not in excess of 100 to 125 r per field and using a moderate voltage technic, in the range of 130 kv. Only one region is treated on any given day and treatments are usually given daily until the leukocyte count has reached the desired level. The original leukocyte count is of primary importance in determining the level to which reduction should be carried. The original count may vary from 30,000 to as much as 600,000 per cubic millimeter of blood. Naturally, the higher levels warrant more consideration in treatment, because of the increased number of cells that must necessarily be destroyed. We believe it unwise if not dangerous to permit the leukocyte count to become too low. We have always felt that in any case of leukemia a mild leukocytosis rather than leukopenia is desirable.

As stated above, the level to which the leukocyte count should be decreased depends largely on the original total count before treatment is begun; also on whether or not roentgen treatment has been given recently. If the count is around 75,000 per cubic millimeter of blood it can be lowered to a level of 25,000 or 30,000. If the original level is higher, approximately 150,000, it should not be reduced to less than about 50,000 at the termination of the course of treatment. If the count is higher than 150,000, it should be lowered to a proportionate level.

In an occasional instance the leukocyte count may seem somewhat resistant to treatment. Such cases deserve careful watching, since the leukocyte count may decrease very suddenly and continue to fall radically for a number of days, even though treatment has been discontinued.

If the urea concentration in the blood has a tendency to increase, we believe the patient should be hospitalized and fluids given intravenously. If the increase in the blood urea is not great, roentgen treatment should be discontinued for several days. We have found that with this procedure the urea will return to a fairly normal level after two to three days and treatment can be resumed.

Since 1935, we have had 23 cases of chronic macrolymphocytic and mesolymphocytic lymphatic leukemia for treatment. Of this group, 17 were of the mesolymphocytic and 6 of the macrolymphocytic type. It is quite impossible to obtain statistics on a group of cases of leukemia since the response varies considerably. In those cases in which treatment was given

in 1935 and 1936, not being aware of the difficulties encountered in this type of leukemia, we used moderately intense treatment. After treatment in several cases we realized that the change in the leukocyte count was so radical that some factors not characteristic of the ordinary chronic lymphatic leukemia must be present. In one particular case an original leukocyte count of 162,000 decreased to 29,300 after only three roentgen treatments given on three successive days. The concentration of urea at the time the leukocyte count was 162,000 per cubic millimeter was 38 mg. per 100 c.c. of blood; after three days, when the leukocyte count was 29,300, the value for blood urea was 86 mg. An example of the response of the leukocytes and the urea under light roentgen treatment is furnished by a case in which the original leukocyte count was 381,000 per cubic millimeter and the concentration of urea 50 mg. per 100 c.c. of blood. At the termination of eight roentgen treatments the leukocyte count was 76,000 and the value for urea 30 mg. Another case that can be used as an example is that of a man forty years old, with an original leukocyte count of 605,000 and blood urea concentration of 48 mg. After a course of ten roentgen treatments the leukocyte count was 99,200 and the blood urea 28 mg. It would be a useless procedure to review all of the cases, since no definite conclusion can be drawn from such a series, but these few examples are cited to show the relative sensitivity of the type of cell found in this particular phase of lymphatic leukemia and the care that must be used in giving roentgen treatment.

SUMMARY

Although the phase of leukemia described above seems rather rare, we believe the therapeutic radiologist should be aware of the dangers encountered in treatment. To safeguard against the possibility of treating this phase of leukemia without adequate consideration we feel that a careful study of the blood smear should be made by a competent hematologist. When the diagnosis has been established, determination of the concentration of urea in the blood is equally as important as the determination of the number of leukocytes. Excessive treatment should not be used because of the dangers of producing leukopenia as well as possible uremia. With adequate care in roentgen treatment, palliation can be brought about in this phase of lymphatic leukemia as well as the usual forms of leukemia for which roentgen treatment is commonly used. Adequate care in this instance means the use of small doses of roentgen rays and frequent determination of the number of leukocytes and the blood urea concentration. Neglect of such precautions can produce fatal results.

The Mayo Clinic, Rochester, Minn.

DISCUSSION

Russell L. Haden, M.D. (Cleveland, Ohio): This paper emphasizes the variation in lymphatic leukemia and the need for studying each patient before treatment is instituted. I am impressed with the great variety of hematologic pictures presented in this type of leukemia. One does not see such a great variation in the myeloid group.

Dr. Popp and Dr. Watkins have stressed, also, the varying reaction to roentgen therapy. Each time I see a patient such as is described here, I wonder if the disease is not more closely related to sarcoma than the classic lymphoid leukemia. Such cells are more responsive to irradiation. The speakers have stated that this fact can be determined from a study of the stained blood film before treatment is begun.

The determination of the blood urea is an excellent point, since the level of urea is a good indication of the degree of toxemia. This seems to come largely from the destruction of body protein. There seems to be a kidney element also, since the products of protein destruction are toxic for the kidney. The fever seen characteristically is also a manifestation of the toxemia.

This paper should make us study the leukemic patient more completely and treat him more intelligently.

U. V. Portmann, M.D. (Cleveland, Ohio): I confess that I am even more confused than Dr. Haden professes to be in the classification of some cases of leukemia. I believe we have not made a separate or distinct classification of the types of lymphogenous leukemia that Dr. Popp and Dr. Watkins have discussed, nor have we treated them differently than others.

I should like to state, however, that we are giving irradiation to many patients in leukopenic stages. We have seen both white and red cell counts improve after treatment. For such cases we usually give spray irradiation anteriorly and posteriorly in small doses—from 25 to 50 roentgens—on alternate days, controlling the total dosage in any period of time by blood counts. We have observed an unfavorable reaction to irradiation in only one patient with lymphatic leukemia. She was given too heavy dosages in too short a time over enlarged cervical and mediastinal nodes in the hope of reducing them so that she could attend her son's wedding the next week. In our efforts to co-operate with her, we created the kind of systemic reaction discussed by Dr. Popp and Dr. Watkins.

R. R. Newell, M.D. (San Francisco, Calif.): I am very enthusiastic about treating all the leukemias with the smallest dose that will produce a result. I should say it might be discreet always to start the treatment with a dose closer to 25 r than 100 or 125, but I don't understand the essayists' apprehension about reducing the white count below 70,000. Even if the white count goes down to 6,000, it seems to me no cause for worry if it has been produced by very small doses of x-ray. I would not strive to drive the count so low, for in a case that is responding well, one expects improvement to continue for some weeks after the course of irradiation has been terminated. But I still see no cause for alarm in the simple fact of a low white count.

Walter C. Popp, M.D. (*closing*): I think one must agree with Dr. Haden that there is probably no clinical entity in which there is more confusion than in the group of lymphatic leukemias. My colleagues and I have used the terms macrolymphocytic and mesolymphocytic in order to distinguish the type of cell that was seen by the hematologist in the smears of the individual cases. We believe this is a distinct entity and should not be confused with leukosarcoma, since leukosarcoma has the clinical features of lymphosarcoma, in which the differential count will show some mild leukemic changes.

My colleagues and I have stressed the importance of frequent determinations of the urea in the blood since we have found that it is not uncommon for this determination to change radically during treatment with roentgen rays. In order to eliminate as much as possible the renal infiltration which might interfere with the output of waste products from the blood stream, we commonly institute treatment to the renal regions so that any renal infiltration, should it be present, can be eliminated.

Further Studies on Radiotherapy of Lymphoblastoma[1]

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New York, N. Y.

THE TERM lymphoblastoma has been suggested by Mallory and defined by Viets and Hunter as a general term for lymphosarcoma, lymphadenoma, Hodgkin's disease, and lymphatic leukemia. Holmes (1) described lymphoblastoma as a progressive generalized disease, occurring at any age, in either sex, and involving any tissues of the body, although primarily it has its seat in the lymph nodes of the neck and the mediastinum.

It is now generally admitted that although there are definite distinguishing characteristics in the clinical manifestations and the histology of lymphosarcoma, Hodgkin's disease, and lymphatic leukemia, there is considerable similarity in their pathogenesis. Thus Ewing (2) believes that mediastinal Hodgkin's disease furnishes a large proportion of cases terminating in lymphosarcoma. Levin (3), analyzing more than 500 cases, frequently found pathological evidence of both Hodgkin's disease and lymphosarcoma not only in the same patient but even in different areas of the same tumor. Warthin (4) reported cases of Hodgkin's disease, and Kato and Brunschwig (5) cases of lymphosarcoma, that eventually developed into leukemia. Evans and Leucutia (6) described three cases of lymphosarcoma which changed into lymphatic leukemia as soon as the bone marrow became involved.

Mueller (7), Sternberg (8), Gibbons (9), Minot and Isaacs (10), Coley (11), Broders (12), and others suggest a close relationship among these three diseases. Some of the authors go so far as to suggest that lymphosarcoma and Hodgkin's disease are phases of leukemia.

Recent experimental data corroborate these clinical observations. Thus in 1936, Parsons (13) reported several dibenzanthracene sarcomas of mice with a coincidental leukemic condition which could be transmitted by grafting of the tumor. This leukemic condition became more obvious with increasing tumor growth and less pronounced with tumor regression. The production of monocytic neoplasms by intrasplenic injections of benzpyrene has been reported by Furth and Furth (14, 15). The close relation between leukemia and lymphosarcoma has been stressed by Richter in his study of mouse leukemia (16). The results of extensive work in experimental leukemia (only briefly mentioned above) leave little doubt as to this relationship.

DIAGNOSIS AND SYMPTOMATOLOGY

It is often difficult to make an exact differential diagnosis of lymphoblastoma because of uncertainty in the clinical picture and variations in the symptoms. Sometimes a suspected case of Hodgkin's disease may turn out to be a case of lymphosarcoma, or *vice versa*.

Lymphosarcoma may arise in one group of lymph nodes or in any lymphoid tissue, such as the tonsils and lymph follicles of the intestinal tract. In the majority of cases, mediastinal lymphosarcoma arises in the anterior mediastinum, but frequently it is found in the vicinity of the thymus.

Lymphosarcoma of the mediastinum grows rapidly and may fill the entire mediastinal space and involve the lungs, bronchi, and other mediastinal organs.

Histologically, lymphosarcoma is a true sarcoma of the lymphoid structure,[2] char-

[1] Accepted for publication in March 1940.

[2] Jeanneney and Dubernat (17) described the difference between lymphocytoma and lymphosarcoma. The former is characterized by normal lymphoid cells without regular arrangement and is limited by an intact capsule. Clinically, however, these tumors are as malignant as lymphosarcoma. Ewing classified lymphosarcoma in two groups: (1) malignant lymphocytoma and (2) reticulum-cell lymphosarcoma.

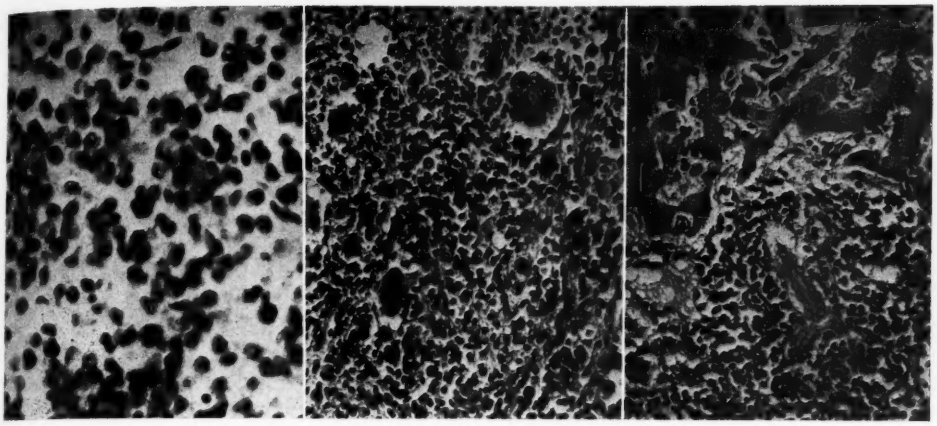


Fig. 1. Lymphosarcoma (reticulum-cell type).

Fig. 2. Hodgkin's disease.

Fig. 3. Lymphatic leukemia.

acterized by reticular basic tissue with embedded lymphoid cells. It must be pointed out that it is never the same as the normal reticular lymphoid tissue because the irregular stroma undergoes more or less fibrotic change and contains an abundance of cells of increased size and of different types. It does not remain confined to the lymph node to form a single tumor of the follicle and node, but breaks through to infiltrate the surrounding tissues. After that the nodes may become matted together (Decker, Leddy, and Desjardins, 18).

In *Hodgkin's disease* the increase in size of the lymph nodes is the dominant feature. During the early phase, the altered lymphatic structure is still recognizable, corresponding to lymphoid hyperplasia. Later, there occurs a multiplicity of cell forms presenting a marked degree of polymorphism, with small lymphoid cells, fibrocytes, granular leukocytes and, particularly, hyperplasia of reticulum cells. Granulomatous lesions are also present, mostly in the spleen, which is usually enlarged.

Leukemia is defined by Boyd as a "condition in which there is proliferation of the leukoblastic tissue either myeloid or lymphoid, as a result of which the proliferated cells may appear in the blood." Accordingly, he distinguishes two types of leukemia, terming them myelogenous and lymphatic leukemias.

In myelogenous leukemia the lymph nodes are only moderately enlarged and rarely acquire the proportions reached in lymphatic leukemia, in which disease mediastinal tumors are not uncommon. Since these tumors sometimes manifest the same physical signs and symptoms as lymphosarcoma or Hodgkin's disease, it may prove difficult to distinguish them from the latter.

In lymphatic leukemia, the spleen is usually enlarged; the same is true of the lymph nodes and other lymphoid tissue. There may also be leukemic infiltrations in any organ of the body, not rarely in the liver and the skin.

Histologically lymphatic leukemia shows hypertrophy of the lymph follicles, which fuse with the pulp cords to transform the entire node into diffuse lymphoid tissue.

A third type of leukemia has also been described. This involves the monocytic cells and is appropriately labelled monocytic leukemia. Kracke and Garver (19), however, studying a large number of cases of monocytic leukemia, pointed out that in all probability it is but an atypical phase of myelogenous leukemia.

Agreement is almost unanimous that in most cases the diagnosis of Hodgkin's disease or lymphosarcoma is impossible

from the blood picture alone (18). Secondary anemia, moderate at first, progressing with the course of the disease, seems to be a constant feature. Desjardins and Ford (20) found leukocytosis more common in Hodgkin's disease than in lymphosarcoma. In some cases of lymphoblastoma (about 5 per cent), however, leukopenia may be present. Initially, normal leukocyte counts occurred in 58.5 per cent, according to these authors. Eosinophilia is rather frequent in Hodgkin's diseases, but is far from constant.

The most reliable criteria for the early diagnosis of leukemia are a preponderance of immature cells, regardless of the total number, and the presence and persistence of specific types of cells such as myelocytes or myeloblasts, as well as a relative and absolute lymphocytosis (Rosenthal and Harris, 21).

Patients with lymphosarcoma and leukemia usually run a low-grade fever. In Hodgkin's disease, however, the Pel-Ebstein remittent type of fever is common; that is, there may be alternating febrile and afebrile periods for weeks and months.

The onset of all three diseases is usually insidious; the patient may be free of symptoms for a long time despite the fact that he is harboring a malignant condition. In the later stages, however, in addition to the general symptoms of weakness, pallor, and loss of weight, the outstanding complaints are pain in the chest, respiratory difficulty, cough, and dysphagia when the tumor exerts pressure on the esophagus. Pressure on the heart may cause palpitations, anginal pain, and inequality of the radial pulse. Pressure on the recurrent nerve produces hoarseness and aphonia. As a rule, however, in Hodgkin's disease, the patient almost from the beginning of the disease manifests cachexia and decline in general condition. In lymphosarcoma, the general condition may remain good for some time (Ewing).

Craver (22) stresses the frequency of puffiness of the eyelids and swelling of the base of the neck associated with mediastinal tumors. Pressure on the large veins produces cyanosis and edema of the face, upper thorax, and upper extremities, with enormous distention of the subcutaneous veins, especially those of the thorax.

The cough is often accompanied by profuse expectoration, sometimes blood-tinged. Hemoptysis is not uncommon, and occasionally there is pleural effusion.

The painless adenopathy which usually accompanies lymphosarcoma, Hodgkin's disease, and lymphatic leukemia is variable. It may be generalized, as in leukemia or Hodgkin's disease, or localized, as in lymphosarcoma. Pruritus, eczema, or other skin condition is not an uncommon early symptom in Hodgkin's disease. In its advanced stage, lymphosarcoma of the mediastinum may perforate the sternum and appear as a tumor on the chest.

The usual complication of lymphoblastoma is involvement of the lungs. Falconer and Leonard (23), analyzing a large number of cases of lymphoblastoma, found that 30 per cent of their patients with lymphatic leukemia, 36 per cent of those with lymphosarcoma, and 31 per cent of those having Hodgkin's disease showed pulmonary involvement. Pleural effusion was present in 65 per cent of the lymphatic leukemia group and 67 per cent of those with lymphosarcoma. These writers emphasize the importance of chest roentgenography at regular intervals.

These data correspond to those given by other authors and are in accord with our personal observations. In 40 per cent of lymphoblastomas treated by us, the lungs were involved to some degree. Three types of pulmonary involvement may be recognized: massive invasion of the lungs by mediastinal lesions, extensions into the lung proper by radiating bands following the interlobular lymphatics, and small isolated nodules scattered throughout the lungs. The frequency of lung involvement makes imperative a complete radiographic examination of the chest.

Roentgen examination of the chest should reveal an abnormal shadow in the thoracic cavity and its origin, and should

indicate whether the abnormal shadow is inflammatory or neoplastic and whether the malignant growth, if present, is primary or secondary.

A specific roentgen picture of Hodgkin's disease in the lung cannot be defined. Lenk (24) states that a clinical picture of tuberculosis combined with roentgen evidence of neoplastic involvement of the lungs is suggestive of Hodgkin's disease.

THERAPY AND PROGNOSIS

Radiotherapy is the only satisfactory, though often merely palliative, treatment for lymphoblastoma. The efficacy of irradiation on lymphoid neoformations is due to the fact that the lymphoid tissue is highly radiosensitive. To quote Ewing (25): "The lymphoid tumors . . . on account of rapid multiplication of cells, loose structure and active metabolism, are among the most sensitive of tumors. . ." Ewing also stresses the fact that these tumors respond best to radiotherapy in patients who are in good general condition. Thymomas form an exception to the rule, since they are radioresistant.

Réné Gilbert (26), confirming the observations of other writers, stated that the biological effect of segmental roentgen therapy on granulomatous tissue is direct; it is cytolytic. According to Ewing, irradiation of affected nodes results in a widespread replacement of cellular tissue by dense sclerosis. Yet, small scattered masses of neoplastic tissue usually survive beneath the capsule of the sclerotic node.

Desjardins (27) found that the radiosensitivity of lymphosarcoma is slightly greater than that of Hodgkin's disease. He emphasizes the fact that lymphoid cells, while extremely sensitive at first, gradually lose their sensitivity after repeated treatment until finally they fail to respond at all. This may be due to a gradual replacement of the lymphoid elements by connective tissue or to the possibility that the cells acquire increased resistance to the effect of the rays.

In accordance with this observation, Decker, Leddy, and Desjardins (18) suggested in the early stage of Hodgkin's disease and lymphosarcoma the administration of a mild dose of moderate voltage (moderate voltage consists of 135 kv., 5 ma., 40 cm. dist., either 2 or 6 mm. Al, 1/4 S.E.D.). Such mild roentgen therapy accomplishes as much as that given with high voltage (200 kv., 5 ma., 50 cm. dist., 0.75 mm. Cu and 1 mm. Al, 1/3 S.E.D.).

Leddy (28) suggested that high-voltage treatment should be restricted to the later and refractory stages of the disease. This principle he recommended in connection with the treatment of chronic leukemia, but indicated that it would apply to all lymphoblastomas.

It is now apparent that in lymphosarcoma, Hodgkin's disease, and leukemia, the involved areas are more numerous and larger than appears clinically. It is not sufficient, therefore, to irradiate only the clinically confirmed areas, but suspicious lesions should be similarly treated. Thus, Dessauer (29) and Wetterer (30) proposed total irradiation of the body. Teschendorf (31) used teleroentgentherapy or total irradiation with good results in cases of chronic leukemia and Hodgkin's disease which had become refractory to local irradiation. The method of teleroentgentherapy merely requires that the roentgen tube be kept at a certain distance from the patient, usually 1.5 to 2.0 meters, in order that the rays may include all or a large area of the body. Gilbert and Babaiantz (32) have elaborated a simple and practical technic for teleroentgentherapy.

Réné Gilbert (33) pointed out once more that roentgen therapy is more useful than radium therapy, except in special cases.

Heublein believed that in order to take advantage of the varying times of mitosis in the tumor cells, total irradiation should be of low intensity, so that it might be given continuously over a comparatively long time. He devised a roentgen-ray therapy ward in which it was possible to administer continuous irradiation to four patients at a time. Behind one wall

of the room a Coolidge tube was placed near the ceiling so that the rays emanating from the tube could reach the patients in all four beds of the ward. His method of continuous irradiation proved of value in radiosensitive tumors, but of little benefit in the resistant types.

According to Cottenot and Sluys (34), teleroentgentherapy is particularly indicated in the neoplastic conditions of the blood and diseases characterized by increased hematopoietic function (polycythemia). They have treated advanced cases of lymphosarcoma, Hodgkin's disease, and leukemia with comparatively good results.

In treating his cases of lymphosarcoma, Cutler (35) not only irradiates the obvious lesions but also all lymph nodes which do not show clinical evidence of disease but are regarded as potentially invaded. His patients receive daily irradiation for four or five weeks. He states that generalized lymphosarcoma may sometimes be controlled for several years.

In entire body irradiation, Edwards (36) uses 200 kv., 30 ma., with 131 cm. distance. Four fields cover one side of the body, and each one receives 25 r. Langer (37) has advocated irradiation of the entire vegetative nervous system, on the theory that hematopoietic lesions are influenced by the quieting effect of irradiation of an "over-irritated vegetative nervous system."

Although we admit that the treatment of choice for lymphoblastoma is irradiation, it is nevertheless shown by experience to be at best palliative, with few exceptions.

"If," Brunschwig and Kandel remark (38), "Hodgkin's disease affects the entire reticulo-endothelial system from the start, little more than palliation can be expected from irradiation. . . . if the process is at first a local one and if the involved group of lymph nodes is discovered on physical examination early in the progress of the disease, intense local irradiation may offer a possibility of arresting the process."

The prognosis of the disease, therefore, depends chiefly on how far the generalization of malignancy has taken place. O'Brien (39), in his report based on ten years' observation of lymphoblastoma in the Boston City Hospital, states that the average survival of patients treated with radiotherapy for Hodgkin's disease is about two years and nine months; for lymphatic leukemia, two years and four months; and for myelogenous leukemia, about three years and two months.[3]

Rosenthal and Harris (21) believe that the treatment of leukemia is largely symptomatic and that roentgen irradiation is the chief means of obtaining symptomatic relief or possible prolongation of life. Of their patients with chronic myeloid leukemia, 35 per cent succumbed in from four to twelve months, 45 per cent lived from two to four years, and a few survived from five to eleven years. The duration of life in chronic lymphatic leukemia was essentially the same; most of the patients lived about a year, a few survived longer, and one patient lived for sixteen years.

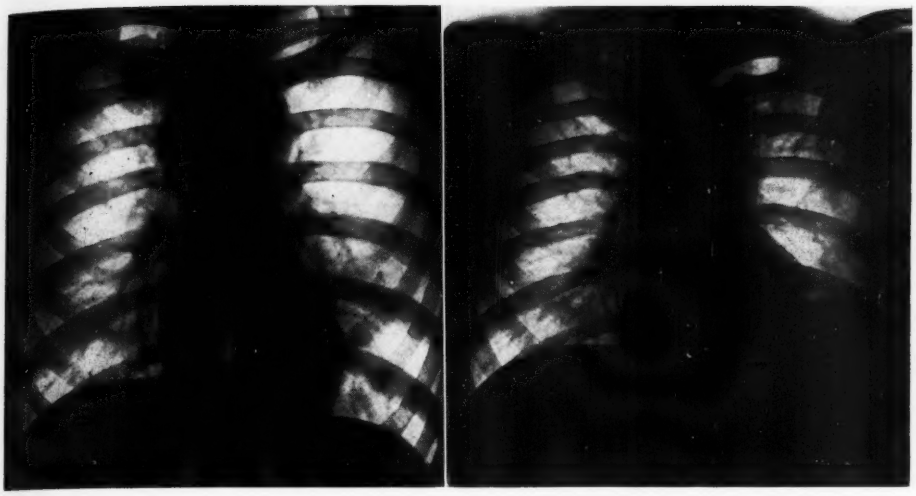
CASE HISTORIES

In the course of ten years we have treated 45 cases of lymphoblastoma, 12 cases of Hodgkin's disease, 15 cases of lymphosarcoma, 13 cases of leukemia, and 5 cases on the border line between leukemia and lymphosarcoma.

We often encountered considerable difficulty in reaching a definite diagnosis, particularly in the beginning, and frequently the course of the disease and its reaction to radiotherapy furnished the only criterion for establishing the precise diagnosis. It is our impression, on the basis of our practice, that the boundaries among these three varieties of lymphoblastoma are often very closely drawn, giving no opportunity for differentiation.

The choice of treatment of the lymphoblastomas is practically limited to roentgen and radium therapy. We found x-ray irradiation more effective than radium,

[3] Our observations of patients with lymphoblastoma gave quite similar figures.



Figs. 4 and 5. Case 1: Hodgkin's disease. The roentgenogram on the left, October 1932, shows slight broadening of the aortic knob, suggestive of lymphatic involvement. The roentgenogram on the right, April 1939, shows density of left hilum; atelectasis of left upper lobe due to pressure of enlarged lymph nodes in the mediastinum or pleural thickening as a result of x-ray therapy. First and second ribs on the left side may present abnormal calcification due to x-ray treatment, possibly calcification of metastasis.

which has been used in a few instances by local application.[4]

CASE 1 (Figs. 4 and 5): Male, 29 years. Onset in May 1932, with enlarged axillary nodes. Blood count normal. Diagnosis: Hodgkin's disease. Medium filtered x-ray therapy. Three symptom-free years, followed by appearance of swellings at base of neck and enlargement of lymph nodes in both axillae. X-ray therapy to mediastinum and involved axillary areas. Slight increase in temperature. Leukocyte count 20,000. Enlarged spleen. Therapy: 12 x-ray treatments over four weeks, to anterior and posterior mediastinum, 100 r per treatment, total 1200 r to each field. Leukocytes reduced to 11,000.

November 1938: Recurrent cervical node swelling; no metastasis demonstrable radiologically. Entire body exposure for two months: 50 to 75 r each treatment; total of 4 treatments, combined with local irradiation to cervical region.

February 1939: Admission with high temperature. Biopsy: Hodgkin's disease. Irradiation to pelvic area, where both inguinal regions showed enlarged nodes.

March 1939: Nodules in posterior occipital region. Residual masses still present in inguinal areas. Irradiation resumed.

November 1939: Recurrent swellings in temporo-occipital region and axillae. Local roentgen irradiation to inguinal and mediastinal areas. Fair physical condition, somewhat anemic.

[4] All dosages are given with back-scattering.

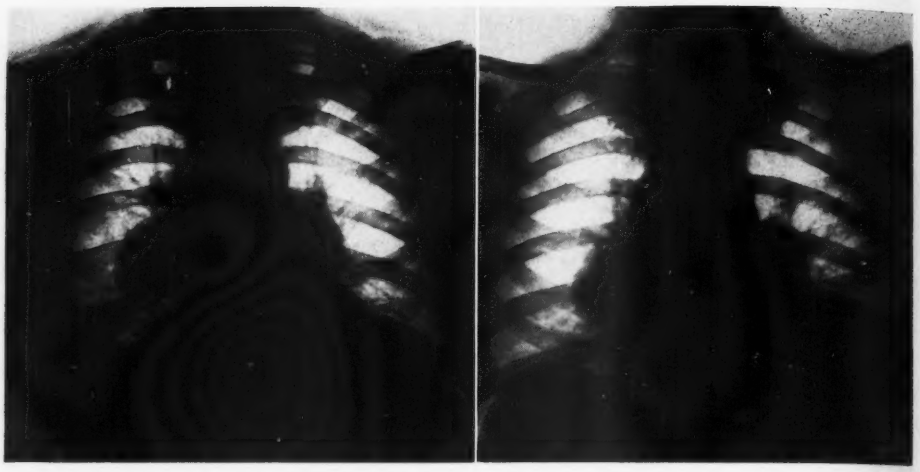
Comment: In the foregoing case life has been prolonged seven years from the onset of the disease, and the patient has not been incapacitated. Within the last year general dyspnea was present. The response to irradiation has become less than previously.

CASE 2: Female, 52 years, admitted July 1936, with loss of weight, swelling of feet and neck for three months. Palpitation, dyspnea, and cough. Spleen enlarged, 3 fingers above symphysis and 1 finger below at median line, 2.5 cm. to right of median line. Liver 3 fingers below intercostal margin. Axillary, cervical, and inguinal nodes present. Wassermann reaction negative. Chest negative. Slight anemia; 9 per cent monocytes. Diagnosis: Hodgkin's disease. X-ray irradiation to spleen and inguinal region, two fields per sitting, 200 r each, three times a week. Total of 800 r to each of 3 splenic fields and 600 r to each of 2 inguinal fields.

August 1936: Re-examination. Spleen almost normal size, slightly hardened; disappearance of nodes in inguinal region.

October 1936: No change for the worse, gain in weight.

May 1937: Almost complete recurrence of previous clinical picture; nodes palpable in both axillae. Second cycle of x-ray irradiation with entire body exposure; favorable response. One year later severe dyspnea and anemia, making further ir-



Figs. 6 and 7. Case 3: Monocytic leukemia before and after irradiation. In the earlier roentgenogram (left) two round masses are seen protruding in mid-portion of right and left hili, evidently due to enlarged mediastinal nodes. Each mass about 2 cm. in diameter. No noticeable changes followed irradiation.

radiation impossible. Death from general emaciation.

Comment: In this case the disease remained radiosensitive but poor physical resources caused premature deterioration. An increased monocyte count has been cited as pathognomonic of Hodgkin's disease, especially if combined with increased eosinophils.

CASE 3 (Figs. 6 and 7): Male, 54 years, referred with diagnosis of lymphosarcoma, February 1939. Past history negative except for fatigue for several months. Wassermann reaction negative. Biopsy refused. No pressure symptoms or displacement of thoracic organs. Blood count normal. Therapeutic irradiation test to intrathoracic lesions, 180 kv., 4 ma., 0.75 mm. Cu and 1.0 mm. Al, 50 cm. dist. Sixteen treatments over 4 fields (2 anterior and 2 posterior) in three weeks, 200 r each treatment. Report by Dr. Held in consultation: "Present differential diagnosis lies between Hodgkin's disease, leukosarcoma, and some other form of benign tumor."

May 1939: Admission for retinal hemorrhage in foveal region. Moderate monocytosis and presence of reticulo-endothelial hyperplasia. Spleen irradiated, 6 treatments over two fields, 150 r per field. Immediate response. Patient under observation with no further sign of progressing pathological process.

Comment: The exact diagnosis in this case is uncertain. Moderate constant monocytosis and retinal hemorrhages are suggestive of leukemia. Goldstein and Wexler (40) reported positive ophthalmoscopic findings in 8 out of 9 cases of leukemia; constant features were retinal hemorrhages and edema of disc.

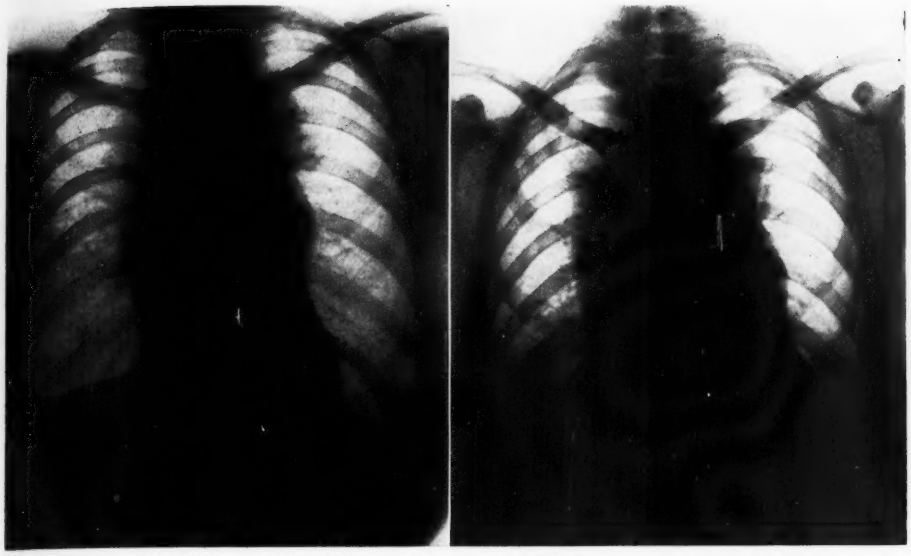
CASE 4: Male, 57 years, with moderate loss of weight. Examination, July 1936. On right side of neck a node about the size of a walnut; other nodes size of hazelnuts. Chain of nodes on left side, one at tip of mastoid 3 cm. in diameter, another size of hazelnut. Several deep-seated nodes along course of Poupart's ligament. Liver slightly enlarged, lower border 3 fingers below costal margin. Spleen somewhat enlarged. Roentgen examination of chest: both apices somewhat obscured by overlying tissue; increased hilar glandular markings. Right costophrenic sinus obscured and straight fluid level at 8th rib. Leukocytes 13,600. Diagnosis: Hodgkin's disease. Irradiation of chest, spleen, and lymph nodes twice daily, 200 r to each field. Total 600 r per area and 3 entire body exposures of 75 r each at 1.5 mm. distance.

September 1936: No palpable nodes in axillary or inguinal areas.

January 1937: Spleen considerably enlarged, liver 4 fingers below costal margin. Hemorrhagic diathesis with bleeding from nose. Blood transfusion. Death the following month.

Comment: This case of Hodgkin's disease responded to x-ray therapy but subsequently became generalized and caused the death of the patient.

CASE 5 (Figs. 8 and 9): Female, 27 years. Complaints: pain in chest, high temperature over three



Figs. 8 and 9. Case 5: Lymphosarcoma before and after irradiation. The pre-irradiation roentgenogram, June 1936 (left) shows considerable broadening of the mediastinal shadow by an irregular mass to the right and left of the mediastinum, overlying the basal region of the cardiac shadow. The trachea is displaced to right. Following irradiation there was a slight decrease in the size of the mediastinal shadow, as shown in the later roentgenogram, November 1936.

months, loss of weight, 10 lb. Tentative diagnosis: lymphosarcoma. Ten x-ray treatments of 280 r per area, over anterior and posterior fields, 10 × 16 cm. Since treatment the patient has felt comparatively well and has gained 64 lb. From time to time swelling occurs, but disappears under x-ray treatment.

August 1939: Hard node size of walnut at apex of armfold in region of anterior border of pectoralis major, diffuse tender swelling, soft, movable, not attached to skin but probably to muscle. Blood count negative except for slight anemia. Biopsy indicated chronic lymphadenitis.

Comment: The clinical evidence in this case at first suggested lymphosarcoma and the patient was treated accordingly. Biopsy, however, showed lymphadenitis. Despite this mistake, treatment should be considered successful.

CASE 6: Female, 58 years, referred in November 1935, with lymphatic leukemia: white cell count 86,000, small lymphocytes 95 per cent. Blindness of right eye of two weeks' duration due to massive hemorrhage in right retina. Diabetes for past twelve years.

December 1935: White cells 202,000; marked anemia. Liver three fingers below costal margin. Nodes in both axillae and in left inguinal region. General weakness, loss of weight. Treatment: insulin, liver therapy, and congo red injections twice a week; x-ray therapy to spleen and areas of node involvement in the groin, combined with entire body exposure.

February 1936: Red cells 3,500,000, white cells 8,600.

October 1936: White cells increased to 60,000. Four treatments given to spleen. Patient seemed to respond well for three months, after which she grew worse and died.

Comment: This case was considered to be grave from the beginning. Though complicated by diabetes and general weakness, the leukemia responded to x-ray therapy and life was prolonged one year.

CASE 7: Boy, 6 years, with history of enlarged cervical nodes at age of four. Blood count at that time showed only slight anemia. January 1932, mastoid operation performed followed by anemia. Leukocytes 21,200. Seen by us February 1932: operative wound unhealed, loss of weight, anemia, and weakness. Three blood transfusions given. Radium pack applied to spleen for 3,000 mg.-hr. and 12 x-ray treatments over the spleen on alternate days, 170 kv., 70 r each. White cells decreased to 8,000, red cells to 1,580,000. Immediate transfusion. Patient died two months later.

Comment: This is an example of acute leukemia, of which persistent earache is

often an early symptom. Operation might have been avoided if a blood study had been done at the time. I reproach myself for giving too intense irradiation in this case but at the time conclusive experience in the dosage for acute leukemia was not available. I believe that lesser dosage at longer intervals would have been of greater benefit and more frequent transfusions might have resulted in prolongation of life.

CASE 8: Male, 29 years. Admission April 3, 1938, with complaint of extreme fatigue, headaches, loss of 30 lb. in three months. Enlarged spleen, 4 cm. below umbilicus, smooth, firm, hard, rounded; notch easily made out. Liver slightly enlarged. Several nodes in right and left inguinal regions. Secondary anemia; white cells 320,000; pronounced myelocytosis; polychromasia; platelets about 150,000. X-ray examination of chest: chronic bronchitis, normal mediastinal shadow. Diagnosis: chronic leukemic myelosis. Spleen irradiated over 3 fields on alternating days, 150 r to each field for total of 600 r per field. Long bones and chest wall received 50 and 75 r once a week. At end of second month white cells 7,700, few myelocytes, secondary anemia. Spleen reduced in size but hard and firm.

June 1938: White cells 27,000. Another radiation cycle to spleen and blood transfusion. At end of August patient's condition satisfactory.

July 1939: White cells 139,000. X-ray treatments given: 80 r to spleen on alternating days to total of 1,800 r. Response satisfactory, although no appreciable change in blood picture (March 11, 1940). Secondary anemia still present.

Comment: This is a typical case of chronic leukemia responding favorably to irradiation of the spleen. Therapy, however, is obviously only palliative.

DISCUSSION

In our study of the reticulo-endothelial system and its relation to malignant growth, we have pointed out (41) that the normal activity of this system is a major factor in resistance against malignancy. The work of Ludford, Foulds, Bruda, and many others, indicates that the resistance to tumor growth which the organism may manifest, may be broken down when the reticulo-endothelial system is blocked and its activity decreased. There appears to be a general agreement that, in some form or another, the protective mechanism against malignant growth depends upon this system which is distributed throughout the body. In malignant diseases of the lymphatic system especially, the activity of the reticulo-endothelial system is of great importance. It is upon this biological premise that the modern technic of radiotherapy of lymphoblastomas is based: protection of the reticulo-endothelial system with a view to preventing generalization of malignancy and the destruction of local lesions with sufficiently strong dosage.

The progress in the treatment of lymphoblastoma in the last twenty years has been great. If, as Réné Gilbert pointed out (42), *life expectancy* has been doubled and even trebled during the last two decades, it must be attributed not only to the perfecting of technic but also to our better knowledge of biological peculiarities of this group of diseases.

The pioneers worked with low-voltage radiation which subsequent radiologists have gradually increased to the present high voltages. At first, massive doses were administered, frequently with disastrous results. The vast destruction of tissue resulted in fatal toxic absorption, the activity of the reticulo-endothelial system was broken down, and so far as the mediastinum is concerned, the resulting edema produced pressure on the vital organs. These unfavorable results led to fractionation of the dose. The importance of the dosage and rhythm of irradiation for the quality of results cannot be sufficiently stressed. In general, the optimal total dose should be the smallest one capable of destroying all the lesions, without jeopardizing the general condition of the patient and without suppressing greatly the function of his reticulo-endothelial system. Considering the great regenerative properties of malignant lymphatic cells, the fractional doses should be given at sufficiently brief intervals to insure uninterrupted radioactivity and to prevent the recovery of malignant cells which have not been completely destroyed,

and the total dose should be high enough to produce complete fibrosis.

With the increased number of autopsies performed on patients who have died of lymphoblastoma, it is evident that the areas of malignant proliferation are more numerous and larger than is clinically suspected. Thus x-ray irradiation should be applied *extensively* to reach not only the lesions clinically or radiologically demonstrable, but also those regions which anatomo-clinical experience shows to be frequently affected by extension of the process. The general reaction and the blood control must, however, be taken into serious consideration.

From our experience we came to the conclusion that radiotherapy must not be repeated except in the presence of a remission. "Safe side" treatment or prophylactic irradiation is superfluous and may be harmful in the absence of active foci of malignant proliferation.

General irradiation should, in our opinion, be used only in selected cases and the dosage should supplement local radiotherapy. Irradiation of the spleen (small dosages, over 3 fields) in leukemic conditions appears to be of considerable value in some cases of lymphoblastoma. Recent experimental work, by Furth, indicates that the involvement of the spleen may be associated with a high incidence of disease in the lungs. He injected into the spleen of mice a small amount of benzpyrene, inducing a leukemic condition in about 16 per cent of the animals. A large number of lung sarcomas appeared among the animals subjected to this splenic treatment.

SUMMARY

Lymphoblastoma should be treated extensively by roentgen rays, with fractional dosage and brief intervals. This treatment, though palliative, may treble the life expectancy of the patient.

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Pancreatic Lithiasis

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PANCREATIC calculi or concretions are rare and are usually found accidentally at autopsy. Clinically their presence is practically never revealed during life. The relatively few cases recognized have been discovered solely by roentgenography.

During the past 270 years 204 cases of pancreatic stones, both operative and non-operative, have been reported, the number increasing from 102 in 1925 to 204 in 1938. This would indicate that the condition is not so rare as formerly believed. Roentgenology has no doubt played its part in the increased accuracy of preoperative diagnosis. Opie found the incidence to be 1 in 1,500 autopsies. It is higher in diabetics—3 cases in 300 autopsies (Warren).

PATHOGENESIS

Calculi are commonly believed to be a sequela to chronic pancreatitis, which itself is usually secondary to biliary tract disease. This leads to stagnation of the pancreatic secretion, out of which the salts are precipitated. As the calculi are mainly composed of calcium carbonate, which is not a constituent of pancreatic secretion, the latter must have been altered, due to the stasis or possibly to infection. Bacteria are believed to play no part except as a secondary factor. The usual belief is that the bile enters the pancreatic duct, causing a subacute and ultimately a chronic pancreatitis. Microscopic examination often reveals a greatly reduced parenchyma and a pronounced endarteritis.

ANATOMY

The pancreas is a long lobulated gland about 12 to 15 cm. in length, which lies almost transversely on the posterior abdominal wall, its right end (head) resting in the concavity of the duodenum and its left end (tail) touching the inferior part of the spleen. Connecting the head and tail is the body, which begins at about the mid-line and crosses toward the left and slightly upward and backward to lie on the left kidney and suprarenal gland. The greater part of the organ lies behind the stomach.

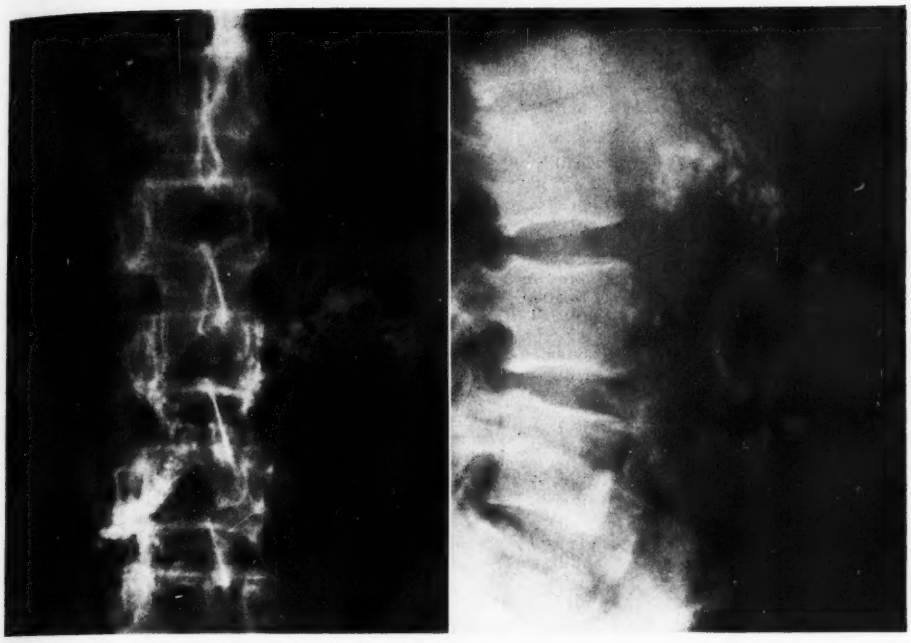
PATHOLOGY

The calculi, commonly multiple, vary in size and shape. They are usually not larger than 1 cm. in diameter. Most often they are very small, resembling sand or gravel. They are dull white in color and are either smooth or rough. As a rule they are irregular and crumble easily, but may be hard. They show usually a high calcium content in the form of the carbonate and phosphate, which accounts for the increased density. The larger calculi may be facetted. They are most often situated in the main duct of Wirsung, less commonly in one of the branches or in the gland substance. They are sometimes branching.

DIAGNOSIS

Significant for the diagnosis is the history of a high alcohol intake, which predisposes to pancreatitis, and attacks of pain brought on by fatty or oily foods. Pain is the most common symptom. The usual finding is recurring attacks of colicky pain in the epigastrium which is apt to radiate toward the left and the back and sometimes to the left shoulder. The pain may resemble gallbladder colic. The next most common symptom is vomiting, coming on at varying intervals after eating. Glycosuria occurs in about 20 per cent of the cases, usually with the

[1] From the Department of Radiology of the Kings County Hospital, Dr. Richard A. Rendich, Director; and from the Department of Radiology of the Brooklyn State Hospital. Accepted for publication in November 1939.



Figs. 1 and 2. Case 1: Posterior-anterior and lateral views.

attacks. Its presence excludes a simple recurring subacute pancreatitis, for in that condition glycosuria is absent. Calcium carbonate or phosphate calculi in the stool are diagnostic. Frothy ill-smelling grayish stools are present only when there is advanced atrophy of the gland. Other symptoms are progressive emaciation and finger point tenderness over the pancreas. Leukocytosis may be found. Jaundice is rare. When present, it is usually mild, unless a calculus is lodged at the ampulla.

Roentgenographically multiple dense calculi may be seen in the normal anatomic position of the pancreas, following the known course of the duct of Wirsung.

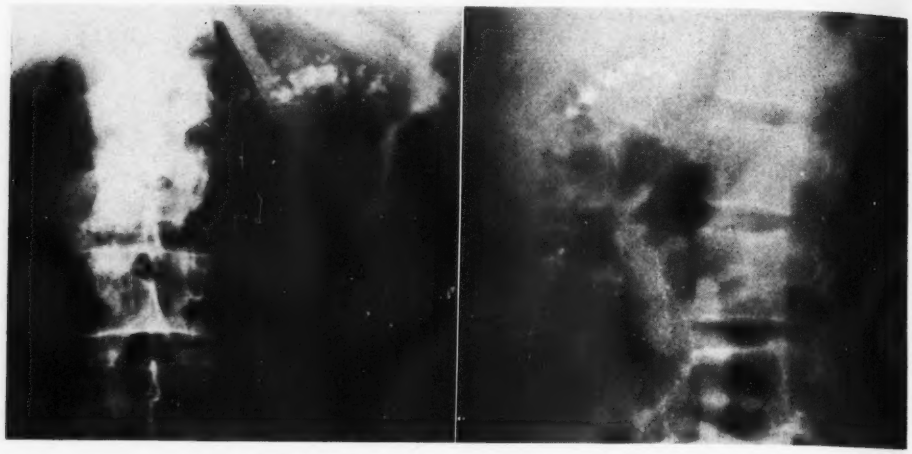
Gillies describes four types of pancreatic lithiasis. (1) The stones may be multiple, irregular, and dense, outlining the entire contour of the pancreas. The stones in the head are lower and on the right; those in the body and tail extend upward and toward the left across the mid-line. (2) There may be a large single calculus. (3) Multiple facetted calculi and (4) large fragmented calculus are rare. The sequelae include retention cysts, atrophy, producing steatorrhea and glycosuria, and acute inflammation with abscess formation.

CASE REPORTS

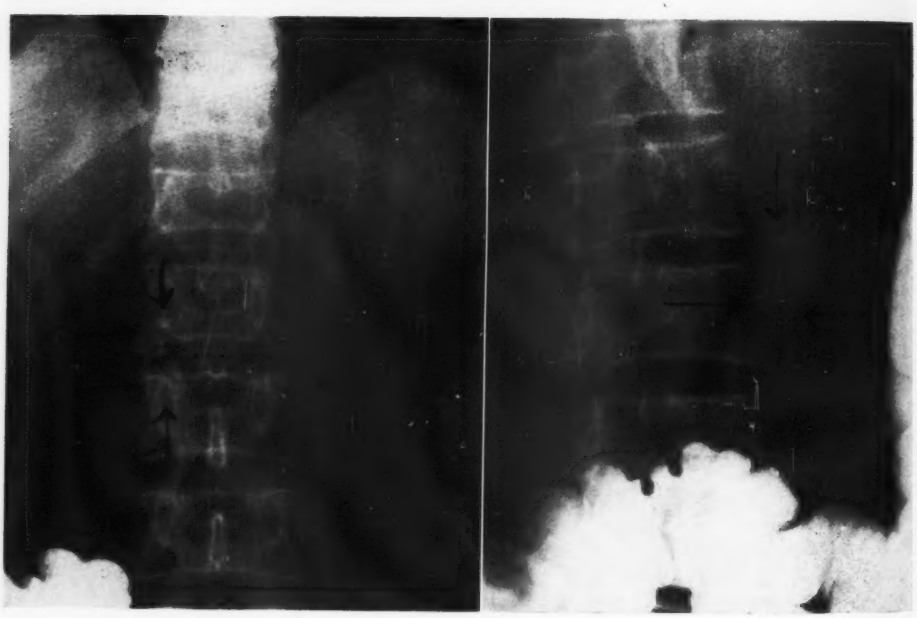
CASE 1: A 54-year-old white man was admitted to the Kings County Hospital in October 1939, complaining of recurrent epigastric pain radiating to the back, for the past twenty years, present two or three hours after eating and relieved by soda; deepening jaundice for the past three months associated with clay-colored stools and dark urine; frequent vomiting at varying intervals after meals; loss of weight, 20 pounds in three months; weakness and anorexia. He had been accustomed to taking large amounts of alcohol daily until three years ago, when a gastro-enterostomy was done for a supposed duodenal ulcer.

The patient was emaciated and jaundiced, with a large liver, a secondary anemia, and a leukocytosis. Roentgen examination (Figs. 1 and 2) revealed multiple small dense irregular concretions distributed uniformly throughout the pancreas and conforming exactly to its true anatomic outline. They varied from the size of pin point to 5 mm. in diameter.

Surgical exploration confirmed the diagnosis, numerous soft chalk-like concretions being scattered throughout the gland. They consisted mainly of calcium carbonate and crumbled easily.



Figs. 3 and 4. Case 2: Posterior-anterior and lateral views.



Figs. 5 and 6. Case 3: Posterior-anterior and lateral views.

CASE 2: A 36-year-old malnourished white man was admitted to the Brooklyn State Hospital in the latter part of 1938 with a diagnosis of alcoholic psychosis and intoxication. During his stay in the hospital he complained of occasional pain in the epigastrium and some tenderness posteriorly, to the right of the mid-line. During a routine gastro-intestinal series, numerous extra-intestinal and extra-biliary calcareous deposits were observed in the upper portion of the abdomen, in the anatomic position of the pancreas. The gallbladder was not visualized after administration of dye.

Laboratory tests revealed a leukocytosis but no glycosuria. The radiographic image (Figs. 3 and 4) was similar to that in Case 1, as to type, number, and position of the concretions.

CASE 3: A white man, aged 45, was admitted to the Kings County Hospital complaining of

crampy abdominal pain and weakness. He had been operated on a few months earlier at another hospital for a malignant growth in the stomach. There was no history of alcoholism. Laboratory data were not significant. Roentgen examination (Figs. 5 and 6) revealed numerous small calculi in the head of the pancreas. The body and tail were free from stones.

CONCLUSION

Three cases of pancreatic lithiasis diagnosed roentgenographically are recorded. This condition has only rarely been discovered during life. Roentgen examination is the only sure means of preoperative diagnosis.

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Tetralogy of Fallot: Contrast Visualization of Heart and Great Vessels[1]

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SINCE THE publication of the pioneering work of Robb and Steinberg (1, 2) on contrast visualization of the cardiac chambers, it has been suspected that an important practical application would be found in the study of congenital cardiac disease. The presence of congenital cyanosis indicates a shunt of the blood flow from the right to the left side of the heart. The exact site of the communication, however, and the size of the right and left ventricles and of the pulmonary artery have been largely matters of inference rather than of precise demonstration. In the following case, contrast visualization was successful in establishing the pathological physiology in a case of tetralogy of Fallot. No similar report has been found in the American literature. A demonstration in two cases was made by Castellanos, Peiras, and Garcia (3), but their observations were limited to the right side of the heart and their studies made in infants exclusively.

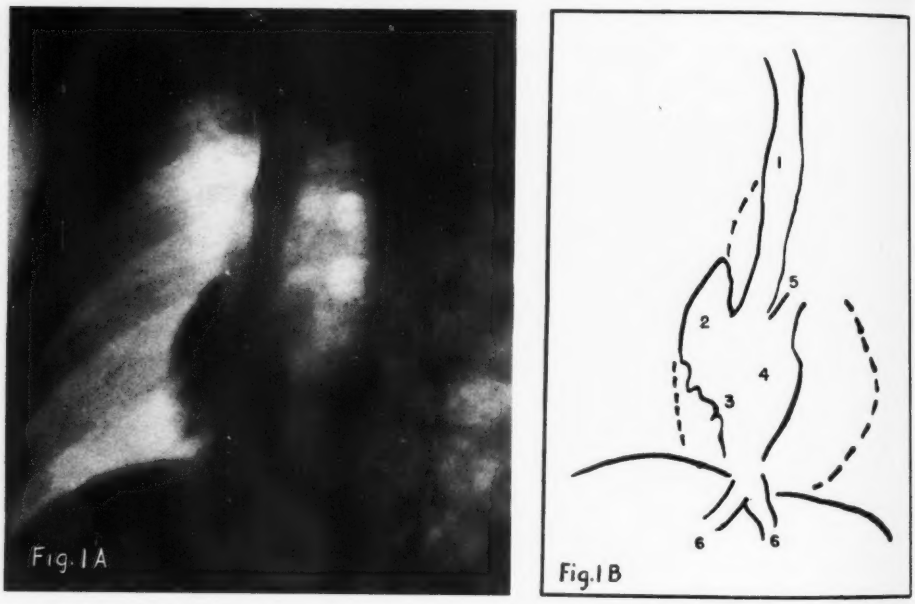

Fig. 1. Visualization of right side of heart, 3/4 second after injection. 1. Superior vena cava. 2. Right auricular appendage. 3. Inflow tract, right ventricle. 4. Outflow tract, right ventricle. 5. Pulmonic conus and valve. 6. Hepatic veins. All illustrations are made in the left anterior oblique position.

N. V. (420,896), a 26-year-old Italian male, has been under observation in the Cardiac Clinic of the Mount Sinai Hospital since birth. He has always been cyanotic, and clubbing of the fingers has been noted since he was first admitted. A loud systolic murmur, heard best over the pulmonic area but also present over the entire precordium, was evident.

[1] From the Departments of Radiology and Electrocardiography, The Mount Sinai Hospital. Accepted for publication in October 1940.

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X-ray examination revealed slight enlargement of the heart to the left. Electrocardiographic examinations showed a regular sinus rhythm, no axis deviation, and a notched P-wave in lead II. No other abnormalities were found. The clinical diagnosis was congenital heart disease, patent intraventricular septum, and pulmonic valve stenosis.

The patient was fairly active and without discomfort until March 1938, when he entered the hospital because of right lower chest pain and dyspnea. This proved to be due to a spontaneous pneumothorax, which completely resorbed in ten days on a conservative régime.

The hemoglobin at that time was 123 per cent, red blood cells 7,090,000. Urine examination revealed no abnormalities. The blood Wassermann test was negative. Chemical examination of the blood also failed to show any abnormalities. The blood volume was 117 c.c./kilo; cell volume 62 per cent; plasma volume 38 per cent. Sedimentation time was over one hour (normal).

Circulation studies (Dr. Wm. Hitzig) revealed: vital capacity 3,500 c.c.; blood pressure 110/85; venous pressure 6.5 cm.; saccharin time 12 seconds; ether time 12 seconds. At 11 seconds the patient complained of generalized "pinching" or "pins and needles" sensations, beginning first in the neck and head and then in the upper extremities and chest. This was followed by similar phenomena in the lower trunk and extremities. These were interpreted as due to a venous-arterial shunt. The occurrence of this reaction in tetralogy of Fallot has been discussed fully by Benenson and Hitzig (4). The phenomenon was repeated precisely on a second injection of ether, but was not obtained when sodium citrate was used as a control. The fact that the ether and saccharin times were equal also justified the assumption of a venous-arterial shunt.

In September 1939, a contrast visualization made by the original method of Robb and Steinberg demonstrated enlargement of the right and left ventricles. The pulmonary artery did not appear to be enlarged. Although there seemed to be simultaneous visualization of pulmonary artery and aorta, the demonstration was not conclusive.

Accordingly in May 1940, the examination was repeated, using both the moving picture (5) and the fluorographic multiple exposure technics (6) with diodrast.[2] These demonstrated: hypertrophy and dilatation of the right ventricle; stenosis of the pulmonary artery above the conus; an intraventricular septal defect below the origin of the pulmonary artery with a right-to-left shunt. The aorta, left ventricle, and pulmonary artery were opacified during the same systole. The left ventricle remained visualized long after the other parts of the heart and the great vessels. Its lumen was much smaller than that of the right ventricle. There was no definite outflow tract from the left ventricle other than through the septal defect. Backflow of the opacified blood into the vena cava inferior and the hepatic veins was noted, suggesting insufficiency of the tricuspid valve.

These observations confirm the diagnosis of tetralogy of Fallot. Complete dextroposition of the aorta (absent aortic conus) can be assumed, and the case classified as type II (Spitzer), or partial transposition (Rokitansky). The absence of right axis deviation in the electrocardiogram of our case suggests complete transposition of the aorta, which gives rise functionally to a cor biatrium monoventriculare. In this way the prolonged opacification, for over ten seconds, of the left ventricle is explained when pulmonary artery and aorta emptied in the normal periods of four and three seconds, respectively. It is assumed that the left ventricle emptied only through the septal defect, presumably by eddy currents.

Fig. 2. Simultaneous visualization of right side of heart, pulmonary artery, and aorta (right-sided aorta), $1^1/_4$ seconds after injection.

SUMMARY

(1) A case of tetralogy of Fallot in an adult with complete dextroposition of the aorta was investigated by the method of contrast visualization.

(2) Pulmonary artery stenosis, intraventricular septal defect with a right to left shunt, hypertrophy of the right ventricle, and dextroposition of the aorta were demonstrated.

(3) The fluorographic multiple exposure technic or the cineroentgeno-

[2] Diodrast solution, 70 per cent, generously supplied by Winthrop Chemical Co.

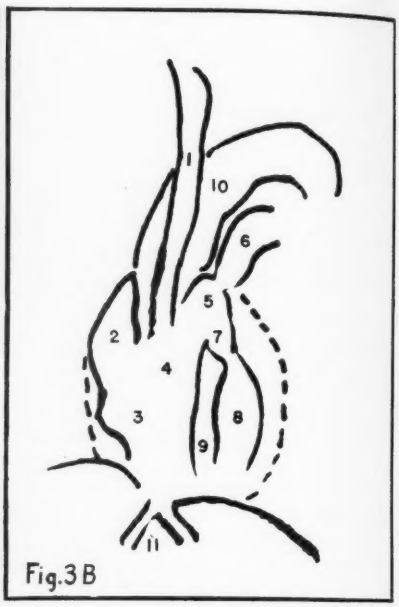

Fig. 3. Visualization of venous-arterial shunt, right to left ventricle (intraventricular septal defect), $1^3/_4$ seconds after injection. 1. Superior vena cava. 2. Right auricular appendage. 3. Inflow tract, right ventricle. 4. Outflow tract, right ventricle. 5. Pulmonic conus and valve, stenosis. 6. Pulmonary artery. 7. Ventricular septal defect. 8. Left ventricle, lumen outlined by contrast media (diodrast) entering through defect. 9. Interventricular septum. 10. Aorta. 11. Inferior vena cava and hepatic veins.

graphic method is essential for successful visualization of all of the features, since only by these means can a sufficient number of exposures be made in a short time.

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Distant Metastases from Carcinoma of the Urinary Bladder[1]

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THE REPORTED occurrences of distant metastases from carcinoma of the urinary bladder are infrequent, since they usually occur late and in a high percentage of cases death intervenes from urinary tract infection long before secondary lesions have had time to develop.

Among 68 recorded cases of carcinoma of the urinary bladder seen at the Kings County Hospital radiotherapy department, there were only 3 in which demonstrable clinical and radiographic evidence of metastases to distant foci was present; a fourth case occurred in the author's practice.

Hinman, in his *Principles and Practice of Urology* (1), writes:

"Metastases as a rule (from carcinoma of the bladder) are relatively uncommon. . . . Metastases by way of the blood stream are more frequent, the osseous system being the organ of predilection." Radiographically these metastatic lesions present no distinguishing characteristics from any other type of lytic carcinoma."

In 1918, Geraghty wrote:

"It is usually noted that the bladder tumors, except in comparatively rare instances, remain well confined to the bladder cavity and do not tend to invade the surrounding structure; nevertheless, metastases to distant points are not infrequent. There are no convincing statistics regarding the frequency of glandular metastases. That the tumors may be very extensive and even deeply infiltrating and still without metastases also occurs. On the other hand, metastases may occur in malignant papilloma in which there is present not the slightest evidence of infiltration of the bladder wall. When metastases occur, the spread to bone seems to be quite frequent. The lungs, liver and spleen are less favorable sites for metastatic deposit."

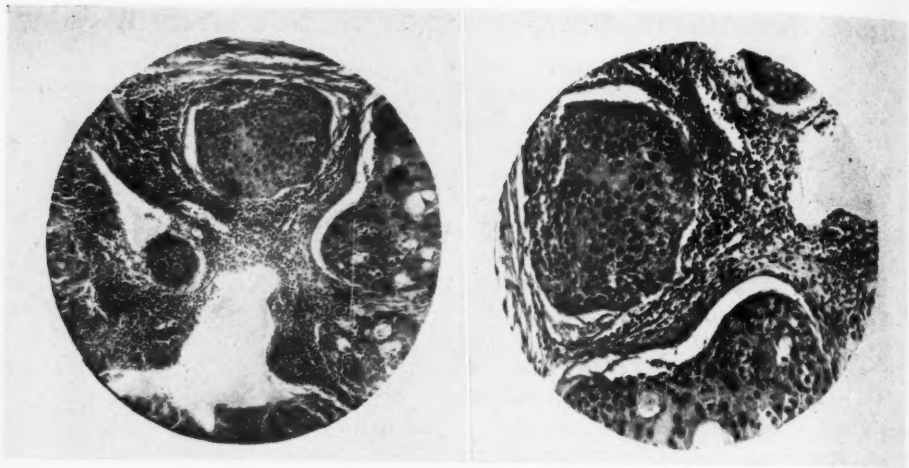
The natural history of epithelial tumors of the bladder is determined by the structure of its mucosa and the physical conditions to which it is exposed. The transitional character of the vesical epithelium, which exhibits both pavement and glandular properties, accounts for the histological varieties of tumors arising from it. The superficial cells are chiefly squamous, while the deeper cells become polygonal and cylindrical. The following classification of bladder tumors is after Hugh Young (3).

I. Mesothelial tumors (rare)
  A. Benign
  B. Malignant
    1. Fibrosarcoma
    2. Leiomyosarcoma
II. Epithelial tumors
  A. Benign
    1. Papilloma
      (*a*) Single
      (*b*) Multiple
      } Pedunculated or sessile
    2. Papillomatosis (one-third to one-half become malignant)
  B. Malignant
    1. Papillary carcinoma
      (*a*) Non-infiltrating
      (*b*) Infiltrating
    2. Non-papillary (flat) carcinoma (always infiltrating)
      (*a*) Transitional
      (*b*) Squamous-cell
III. Secondary tumors: malignant
  A. By extension, *e.g.*, from prostate, cervix, rectum, and colon
  B. By implantation, *e.g.*, from kidney, pelvis, or ureter
  C. By metastasis (extremely rare)

INCIDENCE OF METASTASES

Spooner (2), in an analysis of postmortem examinations of a series of cases seen from 1914 to 1931 at the Mayo Clinic, reported 163 examples of carcinoma of the bladder; of this number, there were 49 which showed definite metastatic foci, distant metastases being found in 24 of these, or 49 per cent. The involvement varied from small scattered foci to extensive destruction of an entire organ. The liver was the commonest site of involvement (14 cases). Following this in order of frequency were the lungs, bones, adrenals, and kidneys.

[1] From the Radiation Therapy Department, Kings County Hospital, Brooklyn, N. Y. Accepted for publication in July 1940.



Figs. 1 and 2. Case I: Metastatic transitional-cell carcinoma of lymph node with metaplasia × 70 and 100.

Figs. 3 and 4. Case I: Diffuse pneumonic type of infiltration compatible with metastatic disease. Fig. 4, the later of the two roentgenograms (right), shows the presence of pleural effusion on the left side.

Spooner further observed that in some of the advanced cases of visceral metastases there was absence of lymph node involvement and little evidence of direct extension to contiguous organs. In the 49 cases presenting metastases, the lymph nodes were involved in 34 instances, or 69 per cent. Metastatic involvement was confined to the lymph nodes in only 12 per cent of the cases.

Spooner comments on the infrequency with which metastatic foci have been demonstrated clinically. Roentgen demonstration of bony metastases from the bladder is rare as compared with malignant lesions of the rest of the urinary tract.

Smith and Mintz (5) examined postmortem the bodies of 34 patients with carcinoma of the bladder and discovered generalized metastases in 47 per cent. The squamous-cell carcinomas were found to have a greater tendency to metastasize than the papillary growths, the ratio being about 2 to 1.

The Committee on Carcinoma Registry (7) of the American Urological Asso-

ciation, in a study based on 902 epithelial tumors of the bladder, found metastases in only 8 per cent. Of the group with metastases, the bones were involved in 47 per cent.

Jenkinson (4), in his case report, expresses the opinion that carcinoma of the urinary bladder as a primary focus for osseous metastases is rare, if available statistics can be considered as an indication of its frequency. "The overwhelming preponderance of prostatic carcinoma over bladder carcinoma as a cause for metastatic bone lesions," he states, "is not in the same ratio as the relative incidence of the primary lesions."

Hyman (8), in a large series of operative cases, found metastatic involvement of the pelvic nodes to be infrequent.

Isolated case reports by Wells (11), Zeman (6), Livingston (9), and others, of metastatic lesions of the bones from primary carcinoma of the bladder, as well as examples of metastases to the brain and lungs appear in the literature.

CASE REPORTS

CASE I: C. M., a 42-year-old Italian female, was seen by her family physician in March 1937, complaining of intermittent hematuria of six months' duration. Associated with this were burning on urination, frequency, and nocturia. There had been a slight loss of weight. Prior to the onset of these complaints the patient's health had always been good. Because of a rather severe recent episode of bleeding, she was referred for cystoscopic examination.

Cystoscopy, in April 1937, revealed a large papillomatous mass involving and filling the greater portion of the bladder cavity. Because of its extent surgery was not considered. A biopsy specimen was obtained and the pathological report was papillary carcinoma, grade 3.

The patient was then referred for high-voltage therapy and between June 5, 1937, and July 8, 1937, received 3,000 r (measured in air) through each of two anterior and two posterior ports (10 × 15 cm.). At the end of treatment, the patient developed a rather severe irradiation cystitis which was soon cleared with daily bladder irrigations. Six weeks following completion of therapy, cystoscopic examination showed no evidence of disease.

The patient continued to do well until October 1937, when urinary symptoms again appeared. Cystoscopy revealed two small areas of recurrence. These were fulgurated. Shortly after this procedure, bilateral supraclavicular, cervical, and axillary adenopathy developed. In the supraclavicular fossae and at the base of the neck were symmetrical clusters of nodes varying in size from 1.0 cm. to 2.0 cm. in diameter, each cluster measuring roughly 6.0 × 6.0 cm. The nodes were resilient and tender. Similar clusters were present in both axillary fossae. Redness and heat were absent.

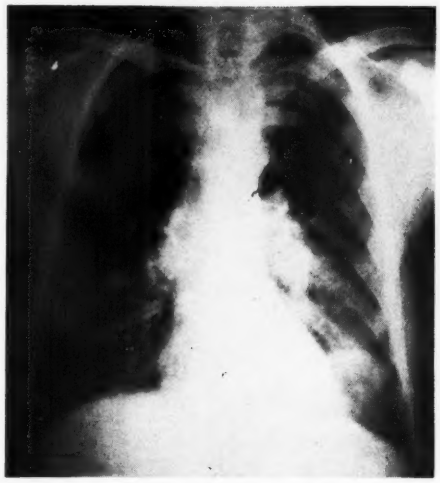


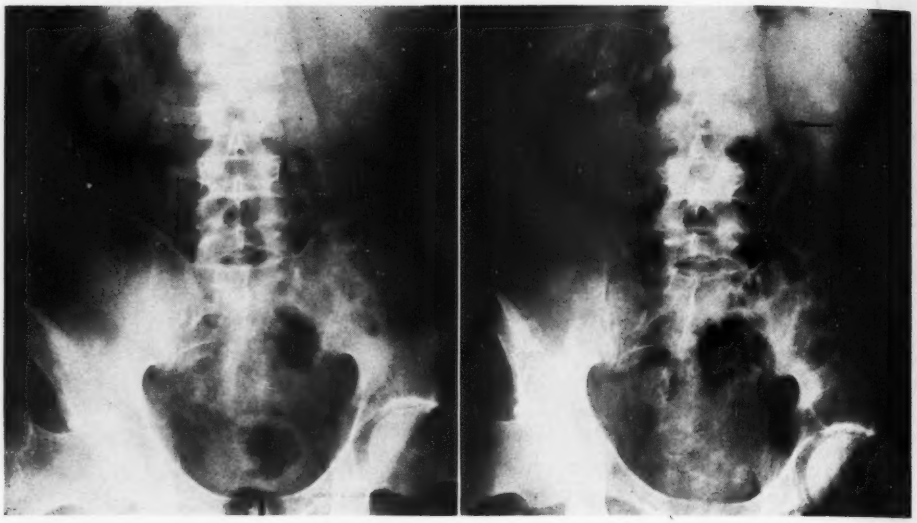
Fig. 5. Case II: Localized spherical areas of consolidation in the lungs.

A biopsy from the left supraclavicular mass revealed metastatic transitional-cell carcinoma (Figs. 1 and 2). X-ray studies of the chest showed a diffuse pneumonic type of infiltration involving both central and basal lung fields, compatible with metastatic disease (Fig. 3). Subsequent x-ray examinations of the chest confirmed the impression (Fig. 4). A pleural effusion of the left chest supervened and malignant cells were recovered from the sediment of the aspirated fluid.

Roentgen therapy was directed to the axillary and supraclavicular masses and the chest in December 1937, for possible palliation. The masses of nodes in the supraclavicular areas receded markedly. Dyspnea, which had been severe, was also relieved. In spite of the palliative effect, however, the patient died in March 1938. Postmortem examination was not obtained.

CASE II: H. V., an Italian male, aged 50 years, was admitted to the Kings County Hospital on the service of Dr. Charles Cochrane in March 1931, with a progressive history of frequency of urination, urgency, hematuria, and dysuria, for five months. Cystoscopic examination revealed a large fungating, ulcerating new growth involving the right lateral wall of the bladder. X-ray examination of the osseous system and chest for metastases proved to be negative.

On April 10, 1931, a suprapubic cystotomy was



Figs. 6 and 7. Case III: Roentgenogram taken on admission (left) showing no evidence of spinal metastases, and later roentgenogram (right) revealing extensive destruction of third lumbar vertebrae.

done. A papillary lesion was found, involving the anterior bladder wall and extending laterally to the right wall, measuring about 3.5 × 4.0 cm. After removing a portion of the lesion for examination, the bulk of the mass was fulgurated. Four platinum tubes of radon were then placed about the periphery of the lesion. A total dosage of 2,114 mc. hours was delivered. The patient remained in the hospital for several months and upon discharge the bladder was entirely free from disease.

Repeated cystoscopic examinations over a period of four and a half years were negative, and the patient remained in good health In April 1935, he was readmitted to the hospital because of cough, recurrent hematuria, generalized weakness, and loss in weight. Cystoscopic examination now revealed a recurrence of the lesion. Roentgenograms of the chest (Fig. 5) showed localized spherical areas of consolidation in both central and basal lung fields, compatible with a diagnosis of metastatic disease of the lungs. The osseous system showed extensive metastatic destruction of the bony pelvis.

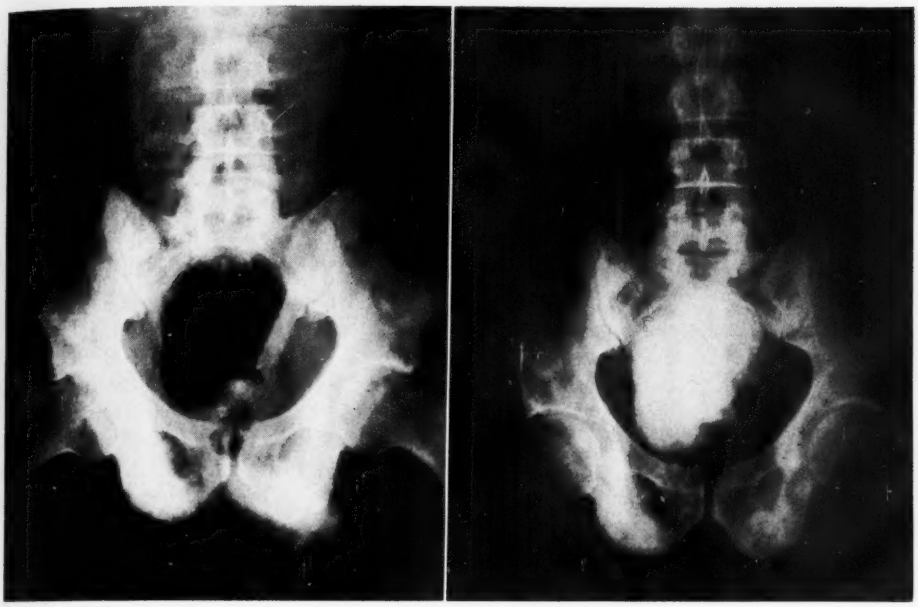
The patient deteriorated rapidly from then on and died six weeks following admission. Postmortem examination was not obtained.

CASE III: E. D., male, aged 57, of German descent, was admitted on the service of Dr. Charles Cochrane in August 1938, with a history of a gradually increasing dysuria beginning one month prior to his admission, difficulty in starting the urinary stream, marked nocturia, and a loss of 20 pounds in weight. There was no gross hematuria. The past history was essentially negative. Cystoscopy revealed an extensive new growth which involved and obscured the left ureteral orifice. Biopsy showed papillary carcinoma. Intravenous pyelography revealed early dilation of the left ureter and kidney pelvis. Function was normal bilaterally.

Because of the extent of the disease and the involvement of the ureteral orifice, a cystectomy was decided upon and in September 1938 a left ureterosigmoidostomy was done with satisfactory result. About six weeks later, the patient began to complain of plain in the lumbar region. Although roentgenograms of the spine, taken upon admission, were negative (Fig. 6), osteolytic metastases to the body of the 3rd lumbar vertebra were now demonstrable (Fig. 7). No further operative intervention was attempted; the patient was referred to the radiation therapy department for intensive treatment. Despite this, he continued to grow worse and died in February 1939. Postmortem examination was not obtained.

CASE IV: W. B., 46-year-old adult male, was perfectly well until January 1940, when he noticed a sudden swelling in the region of the left thigh, which was somewhat painful. He entered a local hospital where a diagnosis of phlebitis was made. Following rest in bed, the swelling slowly subsided and the patient was able to be up and about. A short time thereafter some urinary symptoms developed, with hematuria on one or two occasions. The patient again entered the hospital and, after a thorough survey, a lesion was found in the bladder. No treatment was rendered at this time.

In July 1940, the patient was admitted to Kings County Hospital with a scrotal edema of three days' duration and an increased swelling of the left thigh. Cystoscopic examination revealed an infiltration in the left bladder wall which extended along



Figs. 8 and 9. Case IV: Bilateral pelvic metastases.

the floor of the bladder. X-ray studies demonstrated a constant filling defect of the lateral wall of the bladder on the left side, also involving the floor of the bladder. There was evidence of osteoblastic metastases involving the pelvis bilaterally (Figs. 8 and 9).

A diagnosis of carcinoma of the bladder with bony metastases and probable involvement of the pelvic nodes was made. Microscopic examination of a section of tissue revealed a papillary carcinoma, grade II–III. The patient was referred for radiation therapy.

CONCLUSIONS

Clinically demonstrable metastases from carcinoma of the urinary bladder are rarely recorded because they occur late and in a high percentage of cases death takes place before they have had time to develop.

The extent and amount of infiltration of the tumor are no indication as to the likelihood of metastasis.

Metastasis is by way of the blood stream, rather than through the lymphatic system.

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The Reaction of Kidney Tubules in Tissue Culture to Roentgen Rays[1]

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THE PRESENT report deals with experiments to ascertain whether cells, when in states of physiological activity, are more susceptible to irradiation than when they are not. The tissue used was from the mesonephros of nine- or ten-day chick embryos grown in tissue culture. The amount of irradiation necessary to produce an effect was found to be extraordinarily high. There is a latent period and the intensity of the reaction depends upon the dosage and the condition and type of the cells.

Investigations of the past few years in this laboratory (1) have shown that fragments of kidney tubules of the chick mesonephros continue to function in tissue culture. The secretory activity of the proximal tubules is strikingly shown by their ability to accumulate phenol red from the medium. This suggested a means of testing the effect of x-ray on the secretory mechanism.

The cultures were prepared by placing teased fragments of the mesonephros in hanging drops of a mixture of fowl plasma and Tyrode solution on coverslips and incubating at 37.5° C. After a few hours the cut ends of the tubules heal over, converting the tubules into closed segments which, when secretion occurs, become progressively distended. In some cases the epithelial cells at the cut ends grow out to form sheets extending beyond the explant. In cultures of twenty-four to forty-eight hours the closed segments of proximal tubules within the explanted fragment become distended with secreted fluid. With plasma alone the distention is distinctly less than when phenol red or magnesium sulphate is added to the medium. In the latter case the distention is taken to indicate an enhancement of the secretory process. The outgrowth from the explant consists of wandering cells, fibroblasts, and sheets of proliferating epithelium. The cultures thus provide for a study of epithelial tissue as organized tissue in the form of secreting tubules and as unorganized tissue in the form of outgrowing sheets.

The exposure of the cultures to x-ray treatment necessitated subjecting them to room temperature for about one to two hours. This causes a temporary cessation of secretory activity (1), which is speedily resumed on returning the cultures to body temperature. The controls and experimental cultures were always submitted to the same change of temperature.

The x-ray equipment was a dual tube, self-rectifying machine. This provides two cross-firing beams of x-rays of high intensity and large doses can be administered in a few minutes' exposure. The secondary voltage was kept at 200 kv. and the current passing through each tube was 30 ma. The output intensity, measured in air at the point of treatment (T. S. D. 14.8 cm.) after filtration by the heavy glass tube wall, was approximately 2,700 r/min.

In general, these tissue culture studies deal with the effect of irradiation on secreting and non-secreting renal epithelium, and on other activities of cells, including motility and regenerative processes. Mitoses are not specifically considered in this paper. Spear (2) has an excellent review on this phase of the subject. He

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refers to the greater vulnerability to irradiation of cells in mitosis and ascribes this to their increased activity.

EXPERIMENTAL

EXPERIMENT 1: This experiment was designed to determine the range of sensitivity of the tissue cultures and the lethal dose of irradiation.

Phenol red was added to the cultures at the time they were prepared and the cultures were incubated for forty-eight hours. At this stage the tubules in the explants were well distended with accumulated phenol red. The cultures in this condition constituted an easily detectable means for observing the deleterious effect of the irradiation on the secretory activity of the tubules. The dosages used were 5,000, 10,000, 20,000, 25,000, 40,000, 50,000, 60,000, and 75,000 roentgens administered at room temperature (18–20° C.).

Because of the unavoidable drop in temperature, the tubules of all the cultures had lost some of the accumulated phenol red by the time the irradiation was completed. After two hours of incubation, however, both the control and experimental cultures resumed their activity and showed equal distention and accumulation of phenol red. This was well within a latent period during which no serious effect of the irradiation was ever observed.

Observable effects, if any, became apparent only after a period of twelve or more hours of incubation at body temperature. The effects noted are classified according as they relate to the tubular cysts filled with phenol red or to the cellular outgrowth from the explant.

(*a*) *Effects Observed on the Cysts of the Proximal Tubules in the Explants:* The tubules of non-irradiated cultures maintain their activity for four to five days. After this time the secretory activity of the cystic tubules in the explants slackens. Since the cultures were already forty-eight hours old at the start of the experiments the observations were limited to a period not much longer than the succeeding forty-eight hours.

A dosage of 5,000 roentgens produced no visible effect within forty-eight hours after the irradiation and the cultures did not differ from the controls.

With 10,000 roentgens the cultures appeared healthy and active at twenty-four hours. At forty-eight hours (4 days after explantation), however, many of the phenol-red-filled cysts were paler than those of the controls but the epithelium of the walls still appeared healthy.

With 20,000 and 25,000 roentgens, at eighteen hours, the cysts were already paler than the controls, while at forty-eight hours they retained only a trace of color and were considerably collapsed but with no appreciable change in the appearance of their epithelium.

With 40,000 and 50,000 roentgens there was a considerable loss of color at eighteen hours and the cells in the walls of the cysts showed some vacuolation. At twenty-four hours this cellular degeneration had progressed and at forty-four hours the cysts were completely collapsed and many were entirely cytolyzed.

With 60,000 and 75,000 roentgens the cysts appeared unaffected only during the first twelve hours after irradiation. From then on signs of deterioration became increasingly evident. More and more of the cysts and tubules lost their phenol red and collapsed, while the cells in their walls became heavily granular and vacuolated. At twenty-four to thirty-six hours the cysts were almost entirely cytolyzed.

(*b*) *Effects Observed on the Cellular Outgrowth Beyond the Explants:* The outgrowths, in the order of their appearance, consisted of leukocytes and macrophages, fibroblasts, and sheets of epithelium. The leukocytes and macrophages migrate out in a few hours, followed by the more slowly moving fibroblasts. The epithelium usually does not appear, to any appreciable extent, until after twenty-four hours. In this experiment, the cultures having been incubated for forty-eight hours, there was a considerable outgrowth of wander-

ing cells and fibroblasts at the time of the irradiation.

Cultures receiving 25,000 roentgens showed an immediate toxic effect on all the wandering cells. The leukocytes and macrophages became rounded and darkly granular. Within twenty-four hours after the irradiation they had disappeared from the cultures, apparently by disintegration.

Further outgrowth of fibroblasts was completely inhibited. Instead of rounding up, the cells already present became thread-like and vacuolated and eventually underwent complete disintegration but somewhat more slowly than the leukocytes and macrophages. The epithelium, in contrast to the above, remained healthy and continued to grow with many mitoses for over ten days.

In cultures receiving 50,000 and 60,000 roentgens, only sheets of epithelium survived in the outgrowth, which was more pronounced than in the controls and continued so up to five days after the irradiation.

With 75,000 roentgens the cells of the epithelial sheets appeared normal during the first three days. From then on they became increasingly vacuolated. The sheets then broke into fragments, the cells of which became cytolyzed at the fourth or fifth day. This was long after the cells of the organized tubules had succumbed from the same dosage.

The above experiment was done on cultures to which phenol red had been added prior to the irradiation. The recorded susceptibility of the tubules was, therefore, of cells stimulated to increased secretory activity. When cultures without phenol red were exposed to x-rays, it was found that the tubules were more resistant. Cultures, after twenty-four hours of incubation with closed segments of tubules but without phenol red, could be exposed to 50,000 and even 60,000 roentgens without incurring observable deleterious effects until about forty-four hours after the irradiation. Cytolysis then progressively developed. In contrast to this are the results with cultures irradiated with phenol red present, in which the cysts were completely cytolyzed by this time.

EXPERIMENT 2. This experiment was to determine the effect of stimulating the secretory activity of the cells of the proximal tubules at varying intervals subsequent to irradiation.

The cultures were first prepared without phenol red and incubated for twenty-four hours, by which time the cut ends of the tubules had healed over. The cultures were then exposed to 50,000 roentgens. This dosage was selected because, in the absence of a secretory stimulant such as phenol red, it was found to induce no observable deleterious effects until about forty-four hours after the irradiation. After the irradiation the cultures were allowed to warm up in the incubator and within three hours all appeared to be in excellent condition.

The cultures were now divided into four groups, each group containing 12 irradiated and 6 non-irradiated cultures, the non-irradiated being used as controls. Phenol red was added to each group at different intervals after the irradiation. This was done by removing the coverslips, adding a drop of 0.02 per cent phenol red in Tyrode to each culture, replacing the coverslips, and returning the preparations to the incubator.

Group 1. Phenol Red Added Three Hours After Irradiation: The proximal tubules filled up rapidly with phenol red, the lumina of all the preparations showing rose-colored fluid within one hour. After twenty hours (the cultures being forty-four hours old), a marked change had taken place. The irradiated tubules were much less distended than before and had lost most of their color, the original deep red having changed to a pale pink. The cells of the walls began to show fatty degeneration and many were darkly granular. After twenty-eight hours many tubules were completely collapsed, many were cytolyzed, and only a very occasional small cyst could be found containing even a faint trace of color. After forty-two hours all the proximal tubules were cytolyzed,

although the glomeruli, the distal tubules, and the outgrowing epithelial sheets still appeared healthy. In contrast to this the controls with phenol red and the x-rayed cultures without phenol red appeared healthy and active.

Group 2. Phenol Red Added at Twenty Hours: At this time the cultures still appeared healthy and when the phenol red was added the tubules speedily concentrated it in their lumina. Eight hours later, however, definite signs of deterioration began to set in. Although still in far better condition than those of Group 1, the tubules were inferior to those of the irradiated cultures without phenol red. At forty-eight hours, marked degeneration had taken place and at seventy-two hours the proximal tubules were completely cytolyzed, in decided contrast to the outgrowing sheets of epithelium, which were still in good condition.

Group 3. Phenol Red Added at Twenty-Eight Hours: The tubules at this time appeared healthy and were already somewhat distended. Phenol red, when added became quickly concentrated in their lumina. Eighteen hours later (forty-four hours after irradiation and sixty-eight hours after culturing) only a few tubules were cytolyzed, the healthy tubules showing active concentration of phenol red. This group contained a far larger number of active, proximal tubules than Groups 1 and 2; these were about as healthy as the x-rayed tubules without phenol red, but not as healthy as they had been fifteen hours previously. At seventy-two hours there were only a few living but shrunken proximal tubules containing a pale pink fluid.

Group 4. Phenol Red Added at Forty-four Hours: At this period the toxic effect of the irradiation was already evident. Some of the explants had rounded up, their edges having torn away from the outgrowth. Some tubules were cytolyzed but there were many which quickly picked up some phenol red. Control cultures of this age (ninety-two hours) were in good condition, the explants being well spread out with numerous cysts filled with phenol red.

Conclusions from Experiment 2: The preparations of all four groups at forty-eight hours after irradiation exhibited degeneration of the proximal tubules in direct proportion to the time at which the phenol red was added—the sooner it was added the more speedy the cytolysis.

These results indicate that the secretory renal tubule, when stimulated to secrete, is more sensitive to the delayed effect of x-ray than when it is not. They also show that the sooner after irradiation the tubules are induced to accelerated secretion the more intensive is the destructive effect of the irradiation.

Mention should be made of the segments of the distal tubules. These were found to be the most resistant of all the tissues within the explant to the action of the x-rays. At seventy-two hours after irradiation with 50,000 roentgens they still appeared healthy.

EXPERIMENT 3. *Use of $MgSO_4$ as a Secretory Stimulant:* This experiment was performed by adding $MgSO_4$ (in a final concentration of 0.05 per cent) to the culture medium at the time that the cultures were prepared. After twenty-four hours of culturing, when the stimulating effect of the $MgSO_4$ was well under way and the tubules had become considerably distended, the cultures, with the exception of several kept as controls, were irradiated with a dosage of 50,000 roentgens. Another lot of cultures, prepared without $MgSO_4$, were also irradiated with the same dosage and at the same time.

Fifteen hours later the tubules in the irradiated cultures with $MgSO_4$ were collapsed and deteriorated (Fig. 1-A) while the non-irradiated controls with $MgSO_4$ were healthy and contained many distended cysts (Fig. 1-B). The irradiated controls without $MgSO_4$ maintained their normal appearance until about thirty-six hours after irradiation. Signs of deterioration then set in until, at about forty-four hours, all the proximal tubules had degenerated.

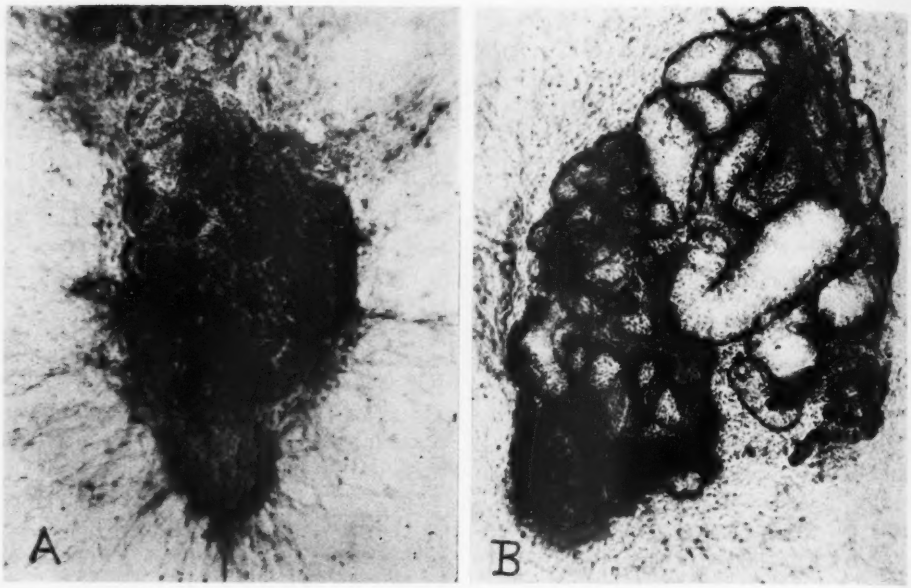

Fig. 1. Cultures of chick mesonephros containing $MgSO_4$ photographed after thirty-nine hours' incubation. A. Irradiated with 50,000 roentgens fifteen hours before being photographed. The tubules are collapsed. B. Non-irradiated control of the same, showing well distended tubules.

In regard to the outgrowing sheets of unorganized epithelium there was no detectable difference between the irradiated cultures of those with and without $MgSO_4$.

EXPERIMENT 4. *Effect of Irradiation on Cellular Repair at the Torn Ends of the Proximal Tubules:* In this experiment the kidneys removed from a ten-day-old chick embryo were irradiated before fragmentation for culturing. This insured x-ray treatment of the tubules before they had been injured by being cut into pieces. One kidney was exposed to 25,000 roentgens while the other was kept as control. Cultures, both with and without phenol red, were prepared from the teased out fragments of both kidneys. The torn ends of the tubules in the cultures of the controls healed over in about two hours.

In the preparations from the irradiated kidney there was little if any repair, so that the majority of the tubules remained open. The cells at the cut ends of some of the tubules became necrotic and the necrosis progressively advanced along the tubules. A very few tubules remained healthy and healed normally.

When phenol red was added at the time of explantation the lack of healing was more pronounced. Observations of these cultures over periods of twenty-four and forty-eight hours revealed extremely few phenol-red-filled cysts, and these were only partially distended. Instead, the phenol red appeared in thin, red lines along the center of a few cylindroid tubules.

A striking feature of the irradiated cultures was the progressive development of unorganized sheets of epithelium arising from the unhealed ends of the tubule fragments. These sheet-like outgrowths were far more extensive than in the controls.

To the cultures which were prepared without phenol red, the dye was added at twenty-four and forty-eight hours. The tubules in these cultures showed more regenerative activity than those given phenol red at the time of explantation. As a result more tubules had healed over and become distended with secretion products. Consequently, there was less unorganized outgrowth of epithelial sheets.

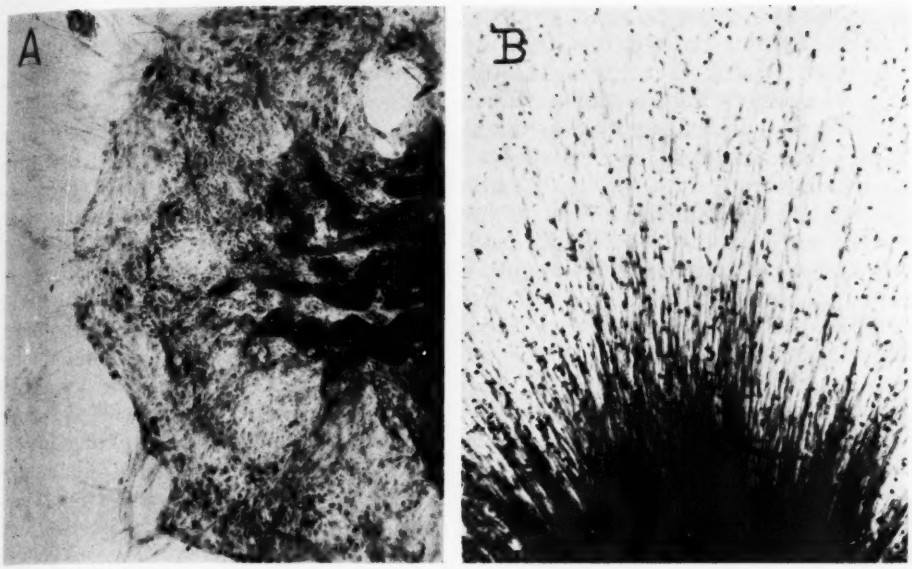

Fig. 2. Cultures showing outgrowth from explant of chick mesonephros after fourteen days' incubation. A. Cultures made from kidney irradiated with 25,000 roentgens. Note widespread outgrowth of renal epithelium and scarcity of fibroblasts and wandering cells. B. Non-irradiated control showing luxuriant outgrowth of fibroblasts and wandering cells with absence of epithelial sheets.

Figures 2-A and 2-B show the contrast between the outgrowths of irradiated and non-irradiated cultures at fourteen days. In the irradiated cultures the outgrowth consisted almost exclusively of renal epithelium, while in the non-irradiated controls (Fig. 2-B) the outgrowth was entirely of fibroblasts and wandering cells, although frequently some epithelium is also present.

DISCUSSION

A significant phenomenon in the irradiation of tissue cultures is the resistivity of the cultures to very high dosages. Hitherto this resistance has been noted particularly in the cellular outgrowth from the explanted tissue. The results of the experiments recorded in this paper indicate that the reparability and the secretory activity of the renal proximal tubules surviving within the explants are also highly resistant, although not to the extent of the epithelial outgrowths from the explants.

The relatively low resistance of a tissue in its natural surroundings in the body of a living animal must be ascribed to an indirect effect of the irradiation on the cells of the tissue. This indirect effect may be due to an impairment of the means of nourishment supply. It may also be due to an irritation causing the abnormal accumulation of leukocytes (3). Neither of these effects applies to tissue cultures, in which there is no circulating blood supply nor any means for the accumulation of leukocytes. In regard to tissue cultures the possibility was considered that irradiation generates toxic principles in the medium. Taylor, Thomas, and Brown (4) found evidence for such a premise in their irradiation experiments on ciliates. They used extremely high dosages—120 to 1,000 kiloroentgens—and ascertained that sufficient H_2O_2 was generated to kill the ciliates provided the medium was water containing sufficient O_2. They found, however, that the presence of agar agar, gelatine, or blood serum in the medium nullified the toxic effect and ascribed this to the catalytic action of the colloids present.

Experiments were made to test the pos-

sibility of toxic substances being produced in the medium of the tissue cultures by transferring irradiated cultures through several changes of fresh medium. When lethal or injurious dosages were used, the transfers were found to have no effect of inducing recovery. It is surmised, therefore, that the irradiation, at least in the tissue cultures, exerts its toxic effect directly on the cells of the tissue and not by way of the medium.

The renal epithelium of the proximal tubule strikingly demonstrates the existence of a susceptibility which varies with the functional state of the cells. As long as the cells are in their normal positions in the wall of the tubule and are secreting, they have been found to be far more susceptible to irradiation than when they are spread out in the form of unorganized sheets of non-secreting cells. It has also been shown that stimulating the secretory activity of the tubular epithelium enhances the destructive effect of the irradiation.

Another significant point is the ability of the renal cells to recover from the effects of irradiation. The cells of a non-stimulated proximal tubule which has been exposed to a sublethal dose will succumb if the cells are stimulated to secrete soon after irradiation. But, if a longer time is allowed to intervene, the cells recover their ability to do the extra work without deteriorating.

The possibility may be suggested that the agents used for stimulating secretion, *viz.*, phenol red and $MgSO_4$, may in themselves be toxic, so that the increase in the destructive action of the irradiation, when the chemical substances are present, is an additive effect of two toxic agents. This would not account, however, for the difference in susceptibility, in the same culture, of the cells in position as columnar secreting cells in the intact tubule and those which have become spread out in unorganized sheets, non-secreting but still viable. A fact worthy of note is the relatively high resistance of the distal tubules, a condition which makes them widely different from the proximal tubules.

Irradiation also pronouncedly affects regeneration at the cut ends of the proximal tubules. In the controls regeneration involves the loosening and proliferation of the cells at the cut ends followed by an alignment of the cells into a columnar epithelium completing the wall of the tubule over its cut end. Whether the movement and the proliferation of the cells are unequally affected by the irradiation was not determined. At any rate, when the tubules are cut into pieces, either immediately before or after a sufficient dose of x-rays has been applied, healing seldom takes place or is abortive. In some cases actual necrosis results with a spread of the necrotic process along the length of the tubule.

A curious phenomenon is that the disorganized epithelial sheets exhibit widespread proliferation which seems actually to be enhanced by irradiation. A stimulation of epithelial growth at certain wavelengths has been reported by Moppett (5).

Regarding the cellular outgrowth, it is to be noted that, of the out-wandering cells, the actively phagocytic macrophages and leukocytes are more susceptible than the less actively ameboid and phagocytic fibroblasts. Moreover, all these wandering cells are far less resistant than the outgrowing sheets of unorganized renal epithelium. This has already been noted by Goldfeder (6), who reported the continued growth of renal epithelium after a dosage of x-rays which caused complete degeneration of the fibroblasts.

The permeability of the wall of the renal tubule may be conditioned not only by the cells composing it but by the material which lies between the cells and by the cuticle surrounding the tubule. It is possible that at least the initial action of an effective dosage of irradiation may be to render the intercellular cement leaky. This possibility is suggested by the fact that the first evidence of deterioration of the phenol-red-filled cysts is a fading of the color in the cysts accompanied by a collapse without observable changes in the morphology of epithelial cells. The lack of healing of the cut

open ends of the tubules without loss of viability of the cells may be related to the lack of cohesiveness of the intercellular material and to the inability of the cells to produce it. The widespread sheets of epithelium proliferating from the open ends of cut tubules in cultures subjected to sublethal doses of x-rays (*e.g.*, 25,000 roentgens) may be the result of a deficiency of the material which holds the cells together in the wall of the tubule.

The results of this investigation show that effective dosages of x-rays disturb the organizing ability of the regenerating tissue in injured regions of the proximal tubule in tissue culture. The results also indicate that cellular activity is a factor in increasing the susceptibility of cells to the lethal effects of irradiation.

SUMMARY

Kidney tubules in tissue culture were irradiated by doses of 5,000 to 75,000 roentgens. Definite effects, within several days of culturing, occurred only with doses of 25,000 roentgens and higher.

Organized secreting tubules and wandering cells were found to be far more susceptible to injury than unorganized epithelial sheets in the cultures. The distal tubules were also found to be highly resistant.

I. Effects on the activity of the proximal tubules:

(*a*) The toxicity appeared only after a latent period during which the tubules gave evidence of continued secretion. The threshold was abrupt, whereupon the tubules progressively degenerated and became completely cytolyzed. The greater the intensity the shorter was the latent period.

(*b*) The susceptibility of the tubules to injury was increased when their secretory activity was stimulated by the addition of phenol red or of $MgSO_4$ to the medium.

(*c*) The susceptibility of the irradiated tubules to secretory stimulation diminished with time. This indicates that the tubules possess recuperative ability.

(*d*) Effective irradiation markedly inhibited the healing over of the cut ends of the teased segments of the tubules.

II. Effects on outgrowing cells:

(*a*) Wandering cells (macrophages and leukocytes) were immobilized and disintegrated.

(*b*) Fibroblasts after exposure to 25,000 roentgens were inhibited from migrating out from the explant. Those which had already grown out did not multiply but became filamentous and vacuolated and finally degenerated. The higher the dosage, the more rapid the cytolysis.

(*c*) Unorganized sheets of renal proximal epithelium were highly resistant and more extensive than in non-irradiated controls. Mitotic divisions were observed in cultures following irradiation with 25,000, 50,000, and 60,000 roentgens.

CONCLUSION

Irradiation of tissue cultures of renal tubules, epithelium, fibroblasts, and wandering cells indicates that the susceptibility of living cells to irradiation is related to their activity, of which the principal forms observed were secretion and motility. The most striking result obtained was the increased susceptibility to x-rays of renal glandular epithelium when a secretory stimulant was applied.

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A Roentgenographic Study of the Relative Incidence of Gastric and Duodenal Ulcer[1]

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THERE IS A RATHER marked discrepancy in published statistics on the relative incidence of duodenal and gastric ulcer. To some extent this may be explained by the different methods of study used, some figures being derived solely from autopsied cases, others being based on operative findings, and still others on clinical observations, with or without roentgenographic examination. Gastric ulcers were formerly believed to be more numerous than duodenal ulcers but today almost all statistics reverse the incidence. The divergence has frequently been explained as being due to faulty clinical diagnosis or to inadequate autopsy technic. Until the advent of x-ray, postmortem examinations were the chief source of information.

Even in the recent literature wide differences are found between the observations of the pathologist and those of the clinician or roentgenologist. In 1938 Portis and Jaffé (8) in a series of 9,171 consecutive autopsies found 455 peptic ulcers, 240 of which were gastric and 215 duodenal. Similarly Stewart (10) found among 1,500 autopsies 130 cases of peptic ulcer equally distributed between those of the stomach and those of the duodenum. Unlike the pathologist, the surgeon and roentgenologist see a greater proportion of duodenal ulcers than gastric ulcers. Thus Mayo (5) reported that at the Mayo Clinic 1,191 patients had been found at operation to have gastric ulcer and 4,532 patients duodenal ulcer, a proportion of 1:4. This may be explained in part by the fact that duodenal ulcers are more likely to produce symptoms severe enough to cause the patient to seek medical or surgical relief than are gastric ulcers with their more silent clinical course. In addition, duodenal lesions tend to be chronic and to occur where the lumen of the gastro-intestinal tract is relatively small. Consequently there is greater tendency to obstruction due to spasm or scar formation.

The study here recorded is based on 4,400 consecutive gastro-intestinal examinations made during the period 1926–1939 at the Colorado General Hospital. Only cases in which the radiologic study confirmed the clinical diagnosis are considered. A total of 883 gastric and duodenal ulcerations were seen, an incidence of slightly more than 20 per cent of the cases examined. Eusterman (2) reports ulcer of the duodenum in 12.2 per cent and gastric ulcer in 1 per cent of a series of 15,985 cases examined by x-ray. Gorman (3) studied radiographically 534 cases and reported duodenal ulcer in 9 per cent and gastric ulcer in 1 per cent. Percy and Beilin (7) in 1,000 examinations found 17.1 per cent duodenal and 2.1 per cent gastric ulcers.

TABLE I: INCIDENCE OF GASTRIC AND DUODENAL ULCER BASED ON ROENTGEN DIAGNOSIS

Total Cases	Duodenal	Gastric
In women 289	215 (74.5%)	74 (25.5%)
In men 594	474 (79.7%)	120 (20.3%)
In both sexes 883	689 (78%)	194 (22%)

Of our 883 cases of peptic ulcer, 689, or 78 per cent, were duodenal, and 194, or 22 per cent, were gastric. Figures in the literature show a wide variation from these percentages. Baetjer and Friedenwald (1) in their study of 743 cases reported 43 per cent duodenal, 40 per cent gastric, and 14 per cent pyloroduodenal ulceration. Sander (9) in 515 cases diagnosed by x-ray examination found 91.5 per cent duodenal

[1] From the Department of Radiology, University of Colorado Medical School and Hospitals. Accepted for publication in August 1940.

5.9 per cent gastric, and 1 per cent gastro-duodenal ulcers. Sutherland (12) of the Mayo Clinic observed an equally great preponderance of duodenal lesions, the ratio being 9:1. In most reports based on roentgen examinations the duodenal ulcer is by far the predominant lesion, just as it is in surgical studies. Undoubtedly, x-ray examination has done much to bring duodenal ulcer to the fore as a popular diagnosis. Lynch (4) states that the records of the Montreal General Hospital for 1917 showed the ratio of gastric ulcers to duodenal ulcers to be 4:1, but in 1926, with the improvement in roentgen examination, the ratio was reversed, with duodenal ulcer becoming the more frequent diagnosis.

Sex: That duodenal ulcers are more numerous in the male is a well recognized fact, but it is often stated that gastric ulcer is more frequently seen in women. This proved to be the case in our series, though as shown in the accompanying table the preponderance is not marked, 25.5 per cent of the women having gastric ulcer as compared to 20.3 per cent of the men, while the incidence of duodenal ulcer was 79.7 per cent for men as compared to 74.5 per cent for women. Among women as a group duodenal ulcerations were found to occur three times as often as gastric lesions. This preponderance of duodenal ulcers is contrary to the results of many studies, but has been corroborated by a study at the Mayo Clinic (11) in which the ratio of duodenal to gastric ulcer among women was 7:1 and among men 6:1, in over 15,000 cases.

In considering peptic ulcer as a whole, men are afflicted more often than women. In our series there were 594 lesions diagnosed in men and 289 among women, percentages of 67.2 and 32.8, respectively. Lynch (4) in his series found 73 per cent of the lesions in men and 27 per cent among women. Sander (9) reported somewhat similar proportions: 68.8 per cent in men and 31.3 per cent in women.

Age: No decade in the life span seems to be exempt from peptic ulcer. It is generally conceded, however, that gastric and duodenal ulcers in women develop at an earlier age than in men. This observation is confirmed in our study as demonstrated in Figure 1. The peak for the

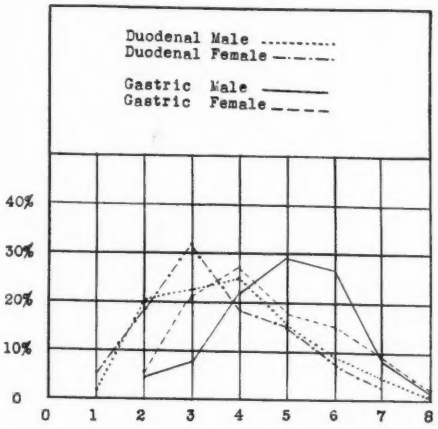

Fig. 1. Incidence of gastric and duodenal ulcer among men and women for the different decades.

incidence of duodenal ulcer in women was in the fourth decade and for gastric ulcer in the fifth decade. Among men the peak of incidence for duodenal ulcer was reached in the fifth decade while the greatest incidence of gastric ulcer was during the sixth decade. Miller, Pendergrass, and Andrews (6) found only 40 per cent of the gastric ulcers among males occurring in the fifth decade as compared with 66 per cent of the gastric ulcers among women. Duodenal ulcer, they concluded, generally occurred at an earlier age than gastric ulcer. Of duodenal ulcers in men 31.7 per cent occurred in the fourth decade. More women were found to have duodenal ulcer (30 per cent) during the fourth decade than during any other.

While this study, based on roentgenographic observations and clinical history, is necessarily less accurate than those based on actual observations at autopsy, it does show that a diagnosis of peptic ulcer was made by x-ray in 20 per cent of the cases in which gastro-duodenal pathology was suspected.

CONCLUSIONS

(1) In a total of 4,400 patients subjected to gastro-intestinal examination 20 per cent were found to have peptic ulcers.

(2) Of 883 diagnosed ulcerations, 689 (78 per cent) were duodenal and 194 (22 per cent) were gastric.

(3) Duodenal ulcer was found to be by far the predominant lesion in both sexes.

(4) The relative incidence of duodenal and gastric ulcers is 3:1 for woman and 4:1 for men.

(5) The peaks of incidence of gastric and duodenal ulcer among women were found to be in the fifth and fourth decades, respectively, while the peaks of incidence of gastric and duodenal ulcers among men were in the sixth and fifth decades, respectively.

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The Roentgen Treatment of Experimental Pneumonia in the Guinea-Pig[1]

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In 1924 the writer with Heidenhain reported 243 cases of acute and subacute pyogenic infections of various kinds treated with roentgen rays. Since that time the effect of small doses of x-rays on inflammations has been investigated by a large number of workers, and as a consequence the method has become an accepted part of roentgen therapy.

The significance of our work lay in the observation that not only did superficial inflammations, such as furuncles, carbuncles, and paronychia react well to x-rays, a fact which had been known for some time, but that inflammations of all types, wherever situated and of whatever cause, were favorably affected. Small doses of roentgen rays were thus shown to be of value even in the deeper lying pyogenic infections, as for example inflammations of the female genital tract and pneumonia. Of especial importance were the observations in pneumonia, showing as they did that not only may x-rays have a life-saving effect, as in postoperative pneumonia, but that they have something to offer when other clinical methods have reached their limit, as in a case of chronic bronchopneumonia which, though unresolved for several weeks, improved in a few days following irradiation, as indicated both by auscultation and roentgen examination (Fig. 1).

A short review of the course of an acute postoperative pneumonia following irradiation may be of interest. A patient with a high fever, severe dyspnea, and cyanosis is irradiated. A few hours later, often within a period of six hours, he states that he can breathe more easily, and he takes some nourishment. After twelve to twenty-four hours the fever abates, in most cases by crisis, breathing is no longer painful, and dyspnea decreases or disappears entirely. In most of the cases reacting favorably a normal condition is reestablished in twenty-four to forty-eight hours. In some cases the fever does not resolve by crisis but falls in two long steps; in some there is a gradual decline to normal. In all these cases the decline

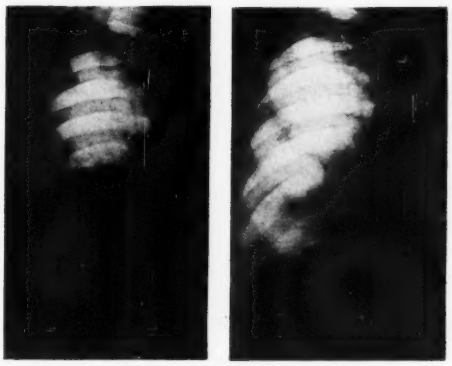

Fig. 1. To the left, an unresolved human pneumonia of the right lower lobe, of four weeks' duration. To the right, the same four days after irradiation.

of temperature, disappearance of dyspnea, general improvement, and indeed the whole course of the disease appear to have been definitely hastened by irradiation. And as this observation was made consistently, it would seem to be an established fact.

Since the course of an irradiated inflammation of any sort is more or less constant, it seemed possible that a study of the course of pneumonia following irradiation might contribute to the explanation of the irradiation effect on inflammations in general. Such experimental investigations as had been carried out by others had been

[1] This paper was prepared during the author's former activity at the Nathan Littauer Roentgen Institute, Breslau. It was presented before the Fifth International Congress of Radiology, at Chicago, September 1937.

limited for the most part to artificially produced wounds, furuncles, or artificial mastitis in the guinea-pig, and showed at best only the histologic changes which take place in the skin and its appendages, or similar tissues, as a result of irradiation. My own earlier experimental investigation, which showed that irradiation increased the bactericides in the blood serum, and which for the first time demonstrated a general effect of irradiation through changes in the blood stream, did not completely clarify the problem. It seemed important to study the effect of irradiation on some deep-seated inflammation, and for this purpose nothing seemed more suitable than pneumonia. The difficulty lay in the choice of a suitable experimental animal and in the artificial production of the disease.

A method was eventually devised whereby a lesion could be produced in the guinea-pig very similar histologically to bronchopneumonia in man. Lack of space prevents a detailed account of the procedure, but in general it consists in the introduction of a definite quantity of bacterial emulsion into the bronchi through the trachea, which is exposed surgically. By suitable positioning of the animal the infecting material is caused to spread out into the lung, where it produces broncho-

Fig. 2. Artificial pneumonia in the guinea-pig. The process in the lung on the left is of 33 hours' duration, unirradiated. The whole lung was of a dark red color, with black flecks of infiltration. The lung on the right, with pneumonia of the same duration, shows the effects of irradiation. The color was for the most part normal with only brownish traces of the infiltrative changes.

Fig. 3. Vertical sections of the lower lobes of the lungs shown in Figure 2. Left: unirradiated, swollen, red, spotted with black. Right: irradiated, normal in appearance.

pneumonia. The experiments have been carried out to date with a suspension of *Staphylococcus aureus hemolyticus* in a dosage which within six hours produces a very definite lesion in the animal but which in no case has proved lethal. This is obviously of importance, since the spontaneous death of the animals would have left no material for comparison, whereas with severe but not fatal infections it was possible to kill both irradiated and unirradiated animals simultaneously at various stages of the disease for comparison. For killing the animals a method was selected which would avoid any effect on the pulmonary tissue.

Fig. 4. On the left, unirradiated spontaneous pneumonia. On the right, normal lung. In the center, irradiated pneumonia, resembling normal lung.

All the animals were gravely ill, as manifested by the fact that for several hours after injection their activity was limited, they huddled together, and with ruffled-up fur sat in the corners of the cages, lost their appetites, and ran a fever. Those irradiated six, twelve, or twenty-four hours after infection, however, in contrast to those which were untreated showed definite clinical improvement. Even though signs of the disease were still present, the animals were less prostrated, or the occurrence of symptoms was delayed, particularly after early irradiation, *i.e.*, within six to ten hours after injection, or the fever was not so high or its appearance was postponed. But these clinical observations, although based on a whole series of animals, cannot be taken as absolute, for individual variations may obscure the actual difference between the irradiated and unirradiated animals. Definite and conclusive differences were observed, however, between the irradiated and unirradiated lungs at autopsy both microscopically and grossly. Animals were sacrificed at various intervals after injection, an irradiated and an unirradiated animal being killed at the same time.

Figure 2 shows the lungs of two animals killed 33 hours after infection. The lung of the unirradiated animal, on the left, is thick and stiff and of a deep red color in both the lower and upper lobes, speckled with darker red and red-black spots. The lung on the right, from an animal irradiated nine hours after infection, shows a normal color and is soft and flabby. In the upper lobe no changes are to be seen but the left lower lobe shows a very delicate brown coloration which we know represents in the irradiated animal the endpoint of the changes which are seen in full development in unirradiated animals. What is taking place is shown in Figure 3, vertical sections through the infected lower lobes of the unirradiated (left) and irradiated animals (right). In the former we have a severe hemorrhagic infiltration (animals are sometimes seen in which the whole pulmonary lobe is thus infiltrated and hepatized); in the sections from the

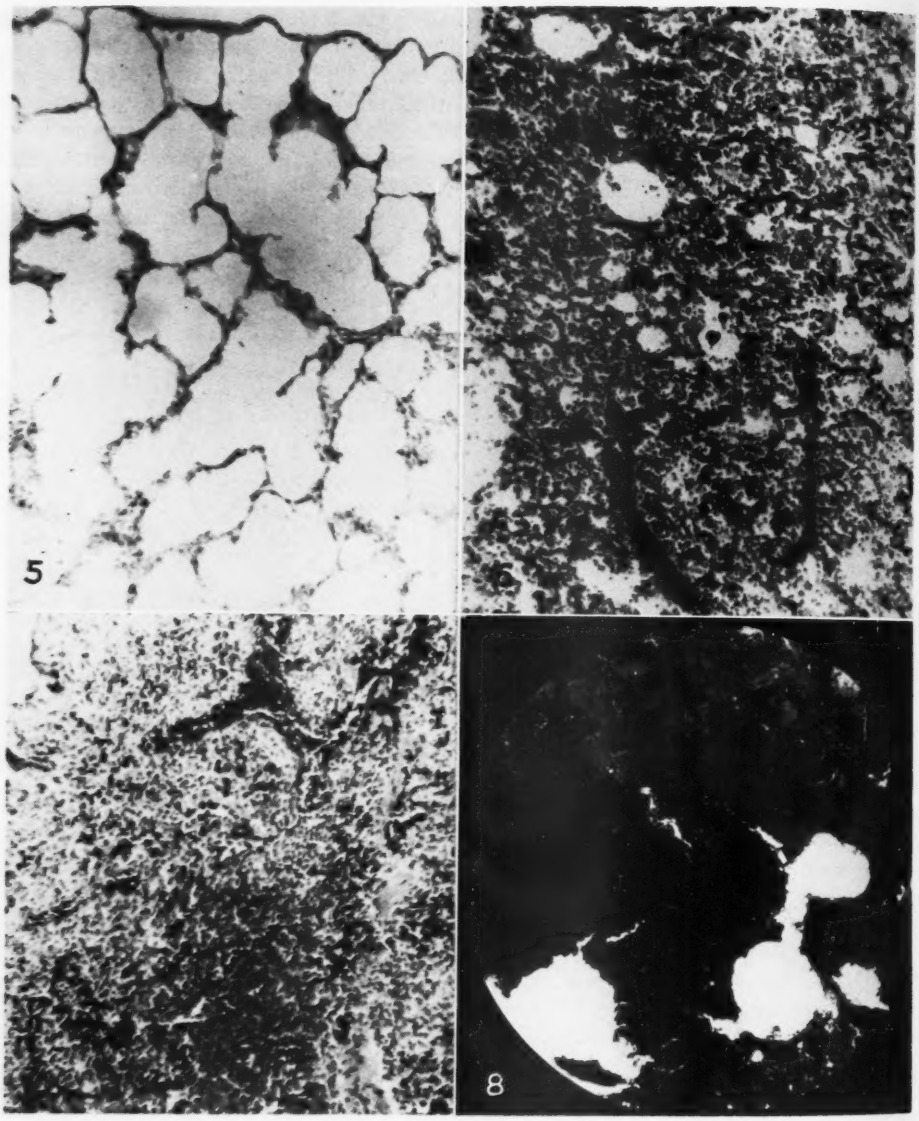

Fig. 5. Section through a non-pneumonic lung, showing wide alveoli and delicate interstitial structures.
Fig. 6. Lung with artificial pneumonia, 19 hours old; compression of the alveoli, vascular congestion.
Fig. 7. Artificial pneumonia, 95 hours old. All the alveoli are compressed and abscesses have formed.
Fig. 8. Pneumonia, 95 hours old. Marked exudation.

irradiated animal, no such change is seen.

In Figure 4 is shown again, on the left, the reddish, darkly spotted lung of an unirradiated animal. Here, though we are dealing with a spontaneous pneumonia, the picture is exactly the same as that of an artificial pneumonia, as shown in Figure 2. On the right is a normal non-infected lung and in the center the lung of an animal killed 48 hours after experimental infection with irradiation 24 hours after infection. The brownish plaques in the lower lobe are again the sole remnants of the pneumonia in the otherwise normal

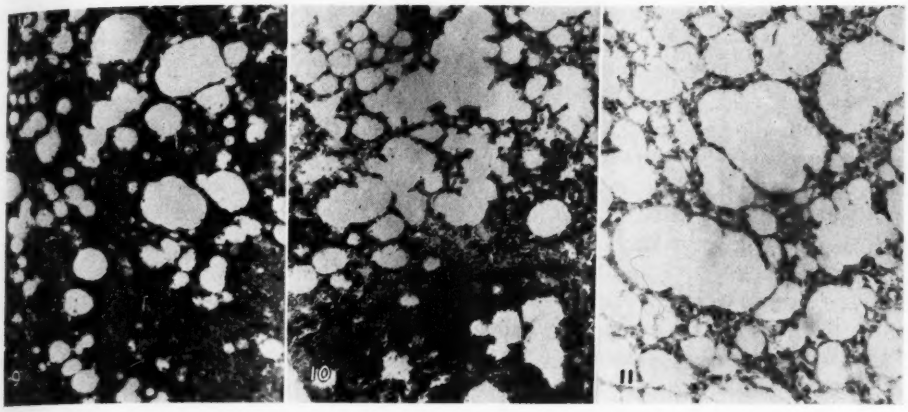

Fig. 9. Pneumonia, 48 hours old, irradiated after 24 hours ("late irradiation"), showing numerous and wide alveoli and infiltration.

Fig. 10. Pneumonia, 48 hours old, irradiated after 6 hours ("early irradiation"), showing slight infiltration, numerous alveoli, and varying degrees of emphysema.

Fig. 11. Same lung as in Figure 10, showing vicarious emphysema.

lung, if we may judge by its color and consistency. These remnants are more marked than in the irradiated lung in Figure 2, due to the fact that irradiation was not carried out until 24 hours after infection. Early irradiation is thus more effective than late irradiation.

It remains to be demonstrated that the microscopic findings correspond with the macroscopic observations, which of themselves are indicative of the effect of irradiation. Figure 5 is a section from a normal non-pneumonic guinea-pig lung showing wide alveolar spaces and delicate interstitial tissue. Figure 6 shows a pneumonic lung 19 hours after artificial infection. The alveoli here are diminished in number; those which are present are compressed by an infiltration of leukocytes and erythrocytes, and the blood vessels are blocked. Figure 7, taken 95 hours after infection, shows the progress of the disease. Alveoli are no longer to be seen; there is a solid infiltration, the vessels are completely blocked, and small abscesses have appeared in the infiltrated tissue. Figure 8, another section from the same animal, shows in addition to the marked infiltrate, a severe exudate such as occurs occasionally in an unirradiated animal.

In the irradiated animals the picture is quite different. If irradiation is carried out twenty-four hours after infection, though local improvement is present, there is still evidence of a severe pneumonia histologically. But whereas in Figure 6, showing an unirradiated pneumonia at 19 hours, almost all of the alveoli present are compressed, in Figure 9, though the disease process is of much longer duration and a still greater degree of compression might be expected, there are present, as a result of irradiation, a great number of functioning alveoli, some of which contain considerable air.

The difference is still more striking if we take for comparison a lung in which irradiation was instituted earlier, *i.e.*, six to ten hours after infection. Figure 10, for example, while showing some severe infiltration (below) shows also (above) many air-containing alveoli, some of them well distended. Figure 11, from the same specimen, shows even more plainly the over-distention of the alveoli and the surprisingly slight infiltration of the interstitial tissue. It should be stated further that in all the photomicrographs of irradiated lungs not only is the interstitial infiltration seen to be less, but, above all, the congestion in the vessels is definitely de-

creased as compared to the unirradiated animals.

Taking these observations all together, it is obvious that radiation hinders the development of pneumonia, particularly when treatment is carried out early; while even if it is performed late, it prevents full development of the disease. Whereas in the unirradiated animal the infiltration increases until finally there is no air surface present in the lung, while abscesses develop and a severe exudate occurs, in the irradiated animal infiltration and abscess formation take place much more slowly and to a markedly less extent, while exudation never reaches the stage that it does in the unirradiated animal. One sees besides in the irradiated animal a "vicarious" emphysema which sometimes fills up the marginal pneumonic lobe, or occasionally even the whole pulmonary lobe. That the irradiated animal is not so dyspneic as the unirradiated one is therefore explained, on the one hand by the inhibition of infiltration and on the other hand by the vicarious emphysema developing after irradiation.

Why the irradiated animals, in contrast to the unirradiated ones, do not die of their pneumonia becomes clear if one compares the marked congestion in the vessels of the unirradiated animals with the lack of congestion and the widening of the vessels in the irradiated ones, which means that cardiac death does not occur in the irradiated animal.

The course of pneumonia in experimental animals is fundamentally the same as the course of a typical postoperative bronchopneumonia in man. I believe, therefore, that I am right in stating that since we have seen in these experiments the effect of x-ray on the infected lung, the result of irradiation in human pneumonia is no chance effect, but is well founded, partly on the definite power of radiation to limit inflammation and partly on its influence on the healing mechanism.

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Effect of Roentgen Irradiation upon Lymphatic Flow in Rats[1]

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THE REACTIONS of tissue to roentgen rays and radium have been studied and described for years. Throughout this time, however, little has been learned concerning the reactions of lymph channels and the flow of lymph to these forms of radiant energy. This may be attributed, as Ewing (1) pointed out, to the difficulty with which changes in lymphatics are followed experimentally. The purpose of the present communication is to report observations on the effect of roentgen irradiation upon lymphatic flow in rats.

The use of thorium dioxide as a contrast medium for roentgen visualization of lymphatics in animals has been described by Menville and Ané (4), and Pomeranz (5). The ease with which colloidal thorium is absorbed by the lymphatics and concentrated in neighboring lymph nodes, where it may be demonstrated roentgenographically, suggested to us its use for studying the adequacy of lymphatic flow following roentgen therapy.

Under normal circumstances 0.05 c.c. of thorium dioxide injected subcutaneously into the hind foot of a rat may almost invariably be seen radiographically in the region of the popliteal or inguinal node within an hour following the injection. If both hind feet are injected simultaneously, the appearance time in the respective lymph nodes is about the same. It seemed reasonable, therefore, to attempt testing the competency of lymphatic flow following irradiation by irradiating one leg and using the contralateral extremity as a control. If the popliteal or inguinal nodes failed to appear on the irradiated side, one might assume that lymphatic flow had been interfered with by the irradiation. If, however, thorotrast could be demonstrated in the nodes on both sides it would seem that irradiation, under the particular conditions, had not influenced the flow of lymph.

White rats were used throughout the experiment. Intraperitoneal nembutal anesthesia was used as a sedative during the treatment, and nembutal or ether while the animals were being radiographed.

One hind leg of each animal was irradiated, the contralateral leg being used as a control. Care was taken to alternate between the right and left legs, so that one-half of the series of rats were treated over the right leg, and the remaining half over the left leg. The animal was protected with lead sheeting, the only region exposed being a small area over the leg between the ankle and the thigh, measuring about 1 cm. square. Two series of experiments were undertaken, one with rays generated at 135 kv., the other at 200 kv.

The first experimental group included 21 rats. The physical factors employed were as follows: 135 kv., 4 ma., 0.25 mm. Cu plus 1 mm. Al filtration, 30 cm. TSD. The total dose delivered to the skin[3] was 2250 r (in air) given at one time in about forty minutes. This produced epilation and a moderately severe skin reaction in the treated area within two weeks after exposure, which healed readily.

Twenty-one to twenty-five days later, under nembutal anesthesia, 0.05 c.c. of thorotrast was injected subcutaneously into the dorsum of each foot. Both sides were either injected simultaneously or the treated side was injected first. Roentgenograms were taken immediately and thereafter at intervals of fifteen to forty-five minutes for a total of forty-five to ninety minutes.

The second group included 16 rats. The physical factors were as follows: 200 kv., 20 ma., 0.75 mm. Cu plus 2.0

[1] From the Department of Radiology and the Robinette Foundation and the Medical Clinic of the Hospital of the University of Pennsylvania. Accepted for publication in October 1940.

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[3] Skin portal 1 cm. square.

mm. Al filtration, 25 cm. TSD. The total dose delivered to the skin[3] was 2200 r (in air) delivered at one time in about twenty minutes. The skin reaction simulated that with rays generated at 135 kv.

Six weeks after treatment, under ether anesthesia, 0.05 c.c. of thorotrast (diluted 1.5 with physiologic saline) was injected simultaneously into the dorsum of each foot. Roentgenograms were taken prior to injection and at fifteen-minute intervals after injection for forty-five minutes.

In the first group of animals thorotrast appeared at the same time on both sides in 10 of the 21 animals injected. In 3 animals the contrast substance appeared on the irradiated side first. In 6 animals thorotrast was seen on the untreated side first. In none of the animals were popliteal or inguinal nodes seen on one side and not on the other. The films of two animals could not be interpreted because the nodes were opaque before thorotrast was injected. It would seem from these data that under the experimental conditions outlined, irradiation produces no appreciable change in lymph flow in the leg of a rat.

In the second group of animals thorotrast appeared at the same time on both sides in 10 of the 16 rats. In one animal the contrast substance appeared on the treated side first. In 3 animals the thorium dioxide appeared on the untreated side first. In none of the animals were nodes seen on one side only. The films of two animals could not be interpreted as they were unsatisfactory. It would seem from these data, also, that under the experimental conditions irradiation produced no appreciable change in lymph flow.

DISCUSSION

Thirty-seven rats were used for the present experiment. In 20 animals thorium dioxide appeared in equal intensity at the same time in the nodes of both hind legs. In 9 animals the contrast substance appeared first on the untreated side, whereas in 4 it appeared first on the irradiated side. That colloidal thorium appeared in some instances a little later on the irradiated side suggests that there may have been a slight interference with lymph flow. In each instance, however, the density of the contrast substance in the nodes eventually became equal.

In 1935 Teneff and Stoppan (6) reported that they could find no evidence of interference with lymphatic circulation following roentgen irradiation. Using rays generated at 180 kv., these men exposed the limbs of dogs to daily doses of 360 to 450 r, the total dose varying from 360 to 6750 r. The patency of lymph channels was tested by means of radiopaque solutions and histologic studies. Our results are in accord with those published by Teneff and Stoppani.

Before the inferences derived from the above experiments may be applied to human problems, much more work is necessary. Different daily doses must be tested, and a much wider range of time intervals after roentgen exposure utilized. Probably of greater significance would be a series of colloid dye studies, using the technic described by McMaster (3), to test rate of lymph flow in irradiated or unirradiated skin areas in man. The preliminary work for this type of study has already been undertaken by Lenz (2).

SUMMARY

In order to determine whether or not roentgen irradiation will interfere with lymphatic flow, the legs of 37 rats were variously irradiated. No significant interference with lymph flow was demonstrated.

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Intraperitoneal Localized Abscess: Roentgenologic Aid in Diagnosis

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LOCALIZED intraperitoneal abscess is a clinical diagnosis which is usually established without difficulty. The history, the localized tenderness, and the high white count are all factors which assist in making the diagnosis. Occasionally, however, cases arise in which the usual methods are not adequate or do not serve to locate the suspected collection of pus. Especially is this true following operations, when three or four surgical possibilities demand consideration and elimination, and we have no clues to the presence or location of an abscess. The most frequent sites for such collections are the retroperitoneal space and the subphrenic space. We shall consider here the less frequent intra-abdominal abscess and suggest some aids in x-ray diagnosis.

Any help we can give the surgeon in localizing an intra-abdominal abscess is of utmost importance, not only from the standpoint of diagnosis but more especially as making possible a direct approach to the diseased area without subjecting the patient to an exploratory laparotomy. We have been fortunate in having been able to furnish such aid in some obscure cases by means of a simple x-ray examination. The x-ray findings in these cases depend on localized ileus; absence of the properitoneal fat line is also of significance.

Alvarez and Hosoi (1) showed by experimental work that irritation of the peritoneum will produce an inhibitory impulse acting on the digestive tract and causing a paralysis of the intestine. An abscess probably acts as such an irritation to the peritoneum and produces an inhibitory impulse affecting the neighboring loops of intestine. In the absence of peristalsis the gas which is normally present in small amounts and which is carried in solution is no longer propelled forward. Stasis occurs, causing the gas and fluid to increase and become visible on the x-ray film (2, 3). We have not under these conditions a true paralytic ileus but the activity of the bowel is inhibited or restrained by an over-active sympathetic influence.

The abscess may cause secondarily an edema of the properitoneal fat, or it may infiltrate this layer of fat. The properitoneal fat is the layer next to the endothelial lining of the peritoneal cavity. On properly exposed films it is seen as a dark stripe. When it is infiltrated with fluid, as may occur in the presence of an abscess adjoining the peritoneal lining, the contrasting dark stripe is lost (4).

These two findings, localized ileus plus obliteration of the properitoneal fat line in the neighborhood, will definitely establish a diagnosis of an intraperitoneal abscess. It may be necessary to take repeated films to be certain that the localized ileus is constant. Indeed, if the diagnosis is obscure and the only positive findings are those demonstrated roentgenologically, it is most important that the examination be repeated, as the consequences of an erroneous diagnosis may be grave, whereas a correct diagnosis may lead to life-saving therapy.

The following four cases demonstrate different conditions in which x-ray examination gave positive diagnostic evidence.

CASE 1: *Acute Appendicitis* This case illustrates some x-ray findings in an acute appendicitis. The appendix had a gangrenous tip which had not ruptured. There was no peritonitis or localized fluid, consequently no reason to expect absence of the properitoneal fat line.

J. R., male, aged 50, had a sudden attack of abdominal pain, not localized, six weeks prior to entry. A similar attack occurred three weeks before entry

[1] From the Surgical Service of Dr. Harold Brunn and the Department of Roentgenology, Mount Zion Hospital. Accepted for publication in May 1940.

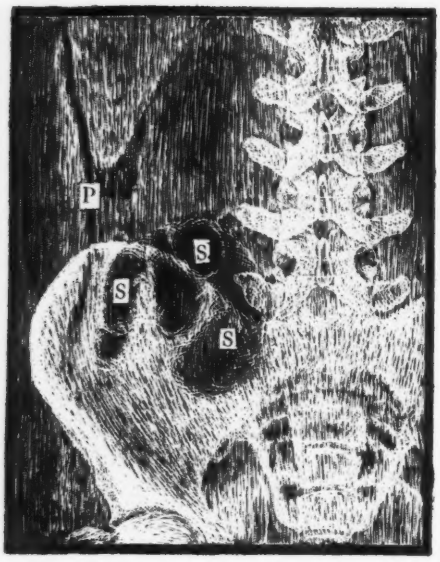

Fig. 1. Case 1: Acute appendicitis. Localized ileus in right lower quadrant. S. Small bowel. P. Properitoneal fat line.

Fig. 2. Case 2: Appendiceal abscess. Localized ileus in right lower quadrant, with absence of properitoneal fat line. S. Small bowel. P. Properitoneal fat line.

and one on the day of admission. The pain became more severe during the day and was associated with vomiting. On the day of admission the pain was localized over the right lower quadrant. Physical examination showed a rigidity in the right lower quadrant with rebound tenderness. The temperature was 37° C., the white cell count 30,000, with 90 per cent polymorphonuclears. X-ray examination (Fig. 1) demonstrated two loops of distended small bowel in the right lower quadrant. The properitoneal line was present. A roentgen diagnosis was made of localized ileus, probably from acute appendicitis. On operation the appendix was found to be acutely inflamed with patches of fibrinous exudate and a gangrenous area at the tip.

CASE 2: *Appendiceal Abscess* (Courtesy of Dr. G. Herzog). A. P., male, aged 57, had a sudden onset of severe colicky pain in the right lower quadrant, spreading over the entire abdomen. This was followed by nausea and vomiting twelve hours later. Symptoms continued for two days before a doctor was called. A physical examination revealed rigidity over the entire abdomen, temperature of 37.6° C., pulse 96, respirations 28. The white cell count was 27,350 with 94 per cent polymorphonuclears. A roentgenogram of the abdomen (Fig. 2), taken in the prone position showed a single loop of distended ileum in the right lower quadrant and absence of the properitoneal fat line in this region, though it was present on the left side and in the upper part of the right side. The diagnosis, on the basis of the x-ray film, was an abscess localized in the right lower quadrant, probably from a ruptured appendix. At operation an appendiceal abscess was found, walled off by omentum.

CASE 3: *Subhepatic Abscess* (Courtesy of Dr. F. I. Harris). The x-ray findings in this case led to a diagnosis of a localized abscess beneath the liver, a complication following a ruptured duodenal ulcer.

J. L., male, aged 42, was operated on for a perforated ulcer. Immediately following the operation his condition improved, but a few days later his temperature rose to 39° C. There were no localizing signs to account for this rise of temperature. Repeated x-ray examinations of the abdomen were negative until the morning of the eighteenth postoperative day. At that time the roentgenogram suggested a diagnosis of localized abscess (Fig. 3). Beneath the liver were a few loops of distended small bowel. A similar picture was obtained in the afternoon and on the next day. The loops of small bowel were lying well above the colon in the region of the subhepatic space. The properitoneal line was absent in the right upper quadrant, though it had been present at previous examinations. It was clearly visible on the left side and in the lower right side of the abdomen. A diagnosis of subhepatic abscess was made. This was confirmed at operation.

CASE 4: *Diverticulitis* (Courtesy of Dr. F. Pearl). J. E., male, aged 84, had lower abdominal pain radiating to the left groin for three weeks. The pain was crampy and intermittent, occurring about every five minutes, with nausea but no vomiting. The white cell count was 20,000 with 88 per cent polymorphonuclears and 12 per cent lymphocytes. A

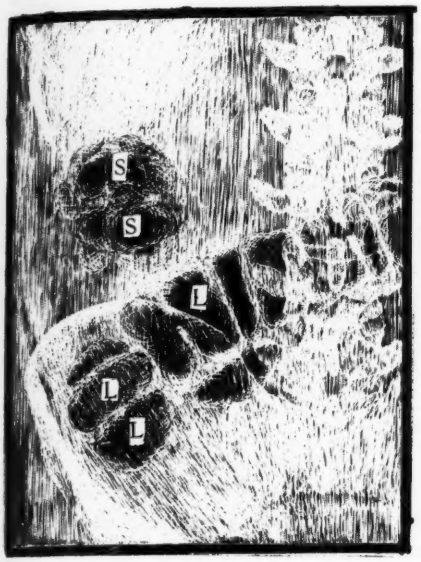

Fig. 3. Case 3: Subhepatic abscess. Localized ileus in right upper quadrant, with absence of properitoneal fat line. S. Small bowel. L. Large bowel.

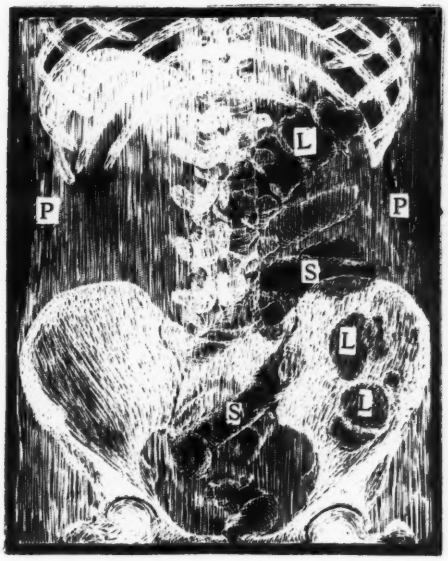

Fig. 4. Case 4: Ruptured diverticulitis. Localized ileus, small and large bowel, in left lower quadrant, with absence of properitoneal fat line. S. Small bowel. L. Large bowel. P. Properitoneal fat line.

mass was palpable to the left and above the umbilicus. X-ray examination showed a few loops of distended small bowel in the left side of the abdomen in the region of the lower descending colon. The properitoneal fat line was absent in this region. The diagnosis was inflammatory mass in the left side of abdomen, probably from ruptured diverticula. At operation a round, smooth, firm mass the size of a baseball was found compressing the bowel. Above and below the mass were multiple diverticula. The final diagnosis was bowel obstruction due to a large diverticulous mass with ruptured diverticula.

SUMMARY

In the presence of symptoms or clinical findings pointing to intra-abdominal pathology the findings described above become very suggestive. We believe they are due to stimulation or irritation of the sympathetic nervous system by inflammation.

This theory of localized ileus receives support from a case recently seen, of a ruptured appendix with a localized abscess of considerable severity. The entire mass was buried beneath the omentum in the false pelvis and the area was covered by a dense congenital band which was adherent to the brim of the pelvis extending over the bladder. In this case the abscess and its products were so isolated from the parietal peritoneum that there was no sympathetic stimulus sufficient to cause an ileus. The position of the appendiceal abscess was such as to prevent infiltration of the properitoneal fat by fluid.

Negative findings such as this must at times be disregarded. On the other hand, the finding of persistent localized ileus together with the history and other clinical facts will give a clue to the diagnosis. If the properitoneal line is also absent we have additional evidence, and a diagnosis of an intra-abdominal abscess can be made with greater confidence.

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A Simple Calculator for Roentgenographic Mensuration[1]

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THE WELL KNOWN relationship between the size of an object and that of its image is given by the following equation,

$$\frac{X}{a} = \frac{H - L}{H} \quad \ldots\ldots\ldots (1)$$

where X is the size of the object, a is the size of the image, H is the distance of the light source to the screen on which the image is projected, and L is the object-screen distance.

In applying the above equation to roentgenographic mensuration, to pelvimetry and cephalometry in particular, it is the object-size that is generally desired. In this case H is the target-film distance and L is the object-film distance. The problem is to find X in terms of the other variables, which are either known or can be easily measured.

The mathematical computation, however, is sometimes considered as time-consuming and laborious. To avoid this, Ball and Marchbanks (1) in applying this equation to the correction of the roentgenographic distortion, devised an instrument, the pelvicephalometer, by means of which the size of the object can be readily obtained when the variables a and L are known while keeping H as a constant. For the construction and use of such an instrument, the original paper should be consulted.

Because this instrument was designed to work at a fixed target-film distance of 30 inches, it is obvious that it cannot be used for other values of H, which depends a great deal on the individual preference of the roentgenologist or the technical limitation of his x-ray equipment. For this reason, Ball (2), in collaboration with Holmquest (3), has recently constructed a calculator in which all the three independent variables, H, a, and L, are incorporated. Essentially, the new calculator consists of a nomographic chart of four linear scales, each representing one variable. Attached to the chart is a movable indicating member with a hair line through the center which can be pivoted at one end to any point along a vertical slot at the center of the chart. By aligning a set of L and H values with this hair line, the position of this pivoting point is determined, from which, when lined up with the image scale, the hair line in turn determines the object size by its intersection with the object scale.

While the ability of this calculator to work on three independent variables is an improvement over the previous one, nevertheless, it suffers from certain disadvantages. One of the chief drawbacks is the non-uniformity of the scales for the target-film distance H and the image size a, thus limiting the accuracy of the instrument. In other words, the degree of accuracy attainable is gradually diminished as the value of the target-film distance and that of the image size are increased. Furthermore, inasmuch as the operation of this calculator is a two-step process, the error introduced in each step will appear in the final evaluation of X, the size of the object. Finally, since accurate alignment of the scales is necessary and the pivoting mechanism has to be precisely made, the instrument cannot be easily constructed and for occasional use many roentgenologists may not be equipped with it.

The present paper reports a simpler calculator which fulfills the same purpose. Apart from its simplicity and accuracy in operation, its construction does not require precision machine work, thus rendering the instrument inexpensive. The uniformity of scale throughout the entire

[1] From the Department of Radiology, Peiping Union Medical College. Accepted for publication in April 1940.

measuring range of each variable offers an additional advantage: the degree of accuracy attainable remains practically unchanged with the magnitudes of these variables used. For the convenience of those who are interested in this work, a chart, considerably reduced, is reproduced here (facing p. 212).

CONSTRUCTION OF THE CHART

To understand the mathematical principle behind the construction of this chart, let us rearrange equation (1) as follows,

$$\frac{X}{a} = \frac{H - L}{H} = 1 - \frac{L}{H}$$

Now let

$$1 - \frac{L}{H} = d$$

Therefore,

$$\frac{X}{a} = d \ldots\ldots\ldots\ldots (2)$$

In this equation, it is seen that d, the correction factor, is uniquely determined as soon as the values of L and H are fixed, being equal to the fraction which is less than unity by the ratio L/H. It is also obvious that this factor d depends on the ratio alone, and that it will remain as a constant so long as the ratio is constant. This means that for each value of the ratio L/H, we can assign to it a value d, the reciprocal of which is the image magnification. Thus when L is equal to zero (the ratio L/H will be also equal to zero regardless of the value of H used), the image magnification will be equal to unity. In other words, there is no magnification at all. This happens when the object is in contact with the film. On the other hand, when the ratio L/H is equal to one, corresponding to the radius vector with a slope equal to unity, the value of d is then equal to zero and consequently its reciprocal will be equal to infinity. This is the case when the object is in contact with the target, thus subtending a solid angle of 2π to the source, causing the image on the film to become infinitely great. In between these two extreme cases, the image magnification varies from one to infinity.

After knowing the exact value of magnification, determined by the ratio L/H, the next step is to get the object-size X from a known image-size a. Mathematically, this is done by dividing the image-size a by the magnification factor or, what amounts to the same thing, by multiplying a by d. This operation can be achieved graphically by means of two families of intersecting curves, one representing the image scale and the other the object scale.

The fundamental requirement that a graph of this type shall perform this operation is that the scales of these two families of curves should be so chosen along a given polar radius that the ratio a/X (image-size/object-size) at the point of intersection shall agree with the magnification demanded by the fixed value of L/H for that radius vector. To construct these curves, one may proceed by one of the two following methods:

1. By keeping the object scale constant throughout the entire range of permissible values of the ratio L/H, varying from zero to one, the image scale is gradually reduced as the ratio L/H is increased. As shown in Figure 1, the family of curves representing the object-size consists of concentric circular arcs with the polar origin as their center, while the other family, representing the image-size, starting exactly with the same scale as that of the object-size on the horizontal axis, converges toward the point O. At this point O, the scale of the image-size is equal to zero. It is seen that the gradual reduction of the image scale radially as one traces upward is a unique function of the ratio L/H: on the horizontal axis, where L/H is equal to zero, the image scale is equal to unity (taking, of course, the object scale as unity), corresponding to a magnification of one; on the radius vector AO_2C, where L/H is equal to 1/2, the image scale is reduced to one half, corresponding to a magnification of two; on the radius vector

AO_1B, where L/H is equal to $3/4$, the image scale is only one fourth corresponding to a magnification of four, and finally when the radius vector takes up the position with L/H equal to one and hence d equal to zero, the same scale is reduced to zero, corresponding to an infinite magnification.

The actual construction of the image curves involves the marking with a pair of dividers of equal distances on the radius vectors as a first step. On a given radius vector, this distance is solely determined by the factor d, being equal to the product of d and the unit length of the object scale. By joining those points indicating the same magnitude of image on the various radius vectors, a family of image curves is obtained.

2. Alternatively, one can construct a polar graph with the image scale kept constant and expanding the object scale with the ratio L/H. In this case, as shown in Figure 2, the family of curves, consisting of a set of concentric circular arcs with the polar origin as their center, represents the image-size, while the other family of curves represents the object-size. These object-curves spread out at first as they go upward from the horizontal axis and then gradually crowd together as they approach the limiting radius vector by a change of curvature from convexity to concavity toward the origin. This peculiar shape is due partly to the nature of the equation and partly to the choice of a point other than the polar origin as their zero point.

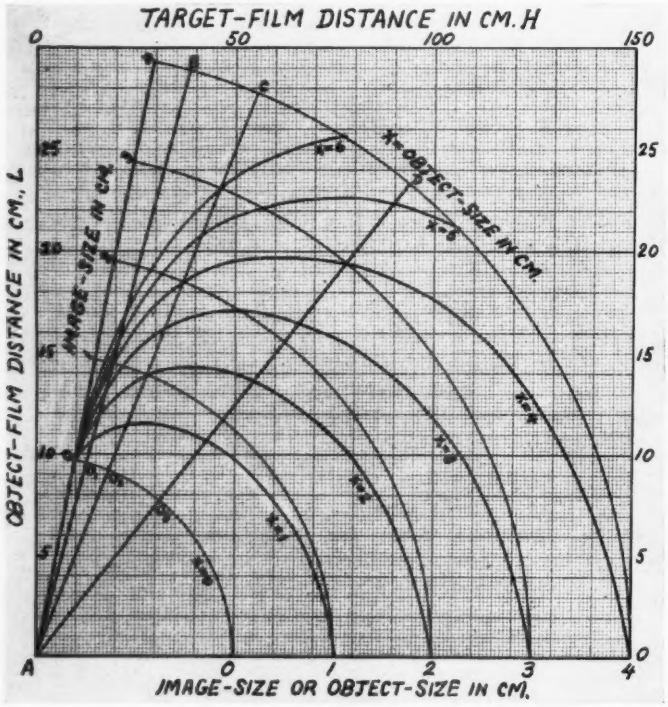


Fig. 1.

The construction of these object-curves is somewhat similar to that of the image-curves in the first method, except that the object scale marked off by the dividers along the various radius vectors is magnified instead of being reduced and that the amount of magnification depends upon the value of the ratio L/H, that is, the slope of the particular radius vector in

question. Thus with the radius vector at the position AO_2C, having a slope equal to 1/2, the magnification is two, because d is equal to 1/2. The proper scale for the object-size, then, at this radial position will be twice that of the image-size; so out of the four units of object scale starting from the horizontal axis only two will remain at this position along the same length of the radius. In a similar way, at the radial position AO_1B, with a slope equal to 3/4, d will be equal to 1/4, so that the object scale will be four times that of the image along this radius vector. By connecting those points indicating the same magnitude of the object on the various radius vectors a family of curves representing the object-size is obtained.

In practice, a movable radial member pivoted on one end to the polar origin is employed. The purpose of using this is twofold: first, it serves as a straight line to set the value of magnification for a given pair of L and H values; second, with the scale clearly marked on this member, it becomes unnecessary to have on the chart the family of concentric circles increasing in magnitude as one reads from the center outward. The presence of these concentric circles would cause much confusion since they must be superimposed on the rectangular graph. The attached scale will indicate the object-size in the first method (Fig. 1) and the image-size in the second method (Fig. 2). In the construction of the accompanying chart the second method has been employed.

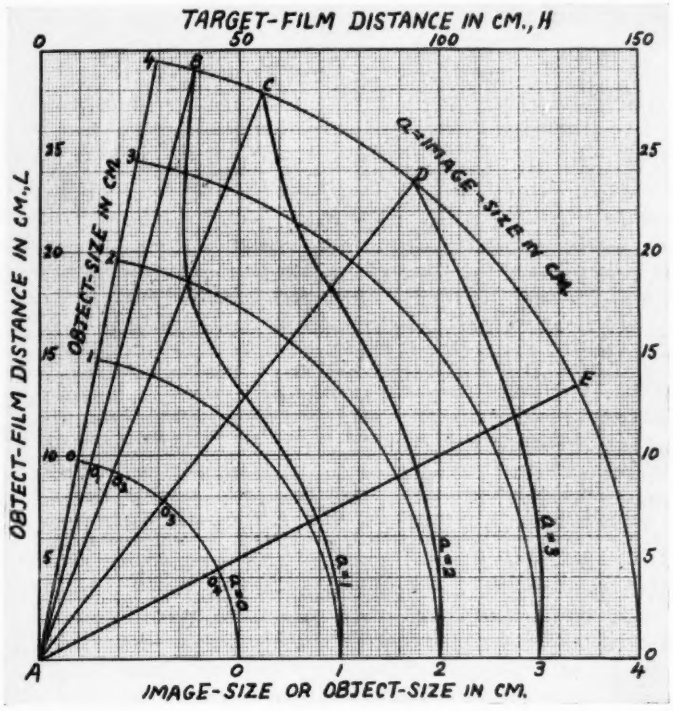


Fig. 2.

An explanation for the adoption of the second method of construction in the chart may not be out of place. In the first method, because of the fact that the family of image-curves converges toward A as the polar radius increases in slope until finally it is almost impossible to identify when the radius lies very close to the

limiting position with a slope equal to unity, the scale is reduced to such an extent that accurate location of the image-size from these curves becomes increasingly difficult. Besides, the additional curves, which do not originate from the horizontal axis and crowd together toward the point A, do not serve any useful purpose. On the other hand, in the second method, the object-scale increases with the value of the ratio L/H, thus permitting the object-size to be located with a greater degree of accuracy.

THE CALCULATOR

Essentially, the calculator is a chart consisting of two superimposed plots; one is rectangular, dealing with the relationship of the target-film distance H and the object-film distance L, while the other is a polar graph of the object-size X on a family of circular arcs indicating the various sizes of the image a. Actually, the circular plot is replaced by a movable radial member which is pivoted on one end to the polar origin. The reproduction in the accompanying insert is approximately one-half the length and one-half the breath of the original chart.

At the bottom of the chart there is a separate strip of scale which indicates the size of the image. This strip should be cut off along the dotted line and mounted on a thin-edged supporting ruler. The chart is then mounted on a flat board for permanent keeping and convenient handling. The ruler with the image scale attached should be pivoted to the polar origin of the chart by means of a precision pin in such a way that the point C' coincides with the point C, thus allowing the radial member to swing freely on the chart. It is important to have the lower edge of the ruler thinned out so that the exact intersection of this image scale with the object scale on the chart can be accurately located. If possible, it is better to use, in place of this ruler, a transparent scale made of exactly the same dimensions, with a hair line through the center. It is essential to have the pivoting point C' in this hair line and at the same time the image scale on the ruler should coincide with the object scale on the chart, when the hair line lies along the horizontal axis.

METHOD OF USE

In practice, a point representing the intersection of the target-film distance used, H, and the object-film distance measured, L, on the rectangular co-ordinates is first noted.[2] Next, swing the movable radial member to this point, and note the point on the scale of this radial member which corresponds to the image-size a and the curve that meets this point. By tracing this curve downward until it intercepts the horizontal axis, the net size of the object can be obtained from the adjoining table at the bottom of the chart. This table also contains the volume of a sphere calculated from a measured diameter or circumference, which may be used in the evaluation of the pelvic or fetal sphere when the diameter or circumference is known.

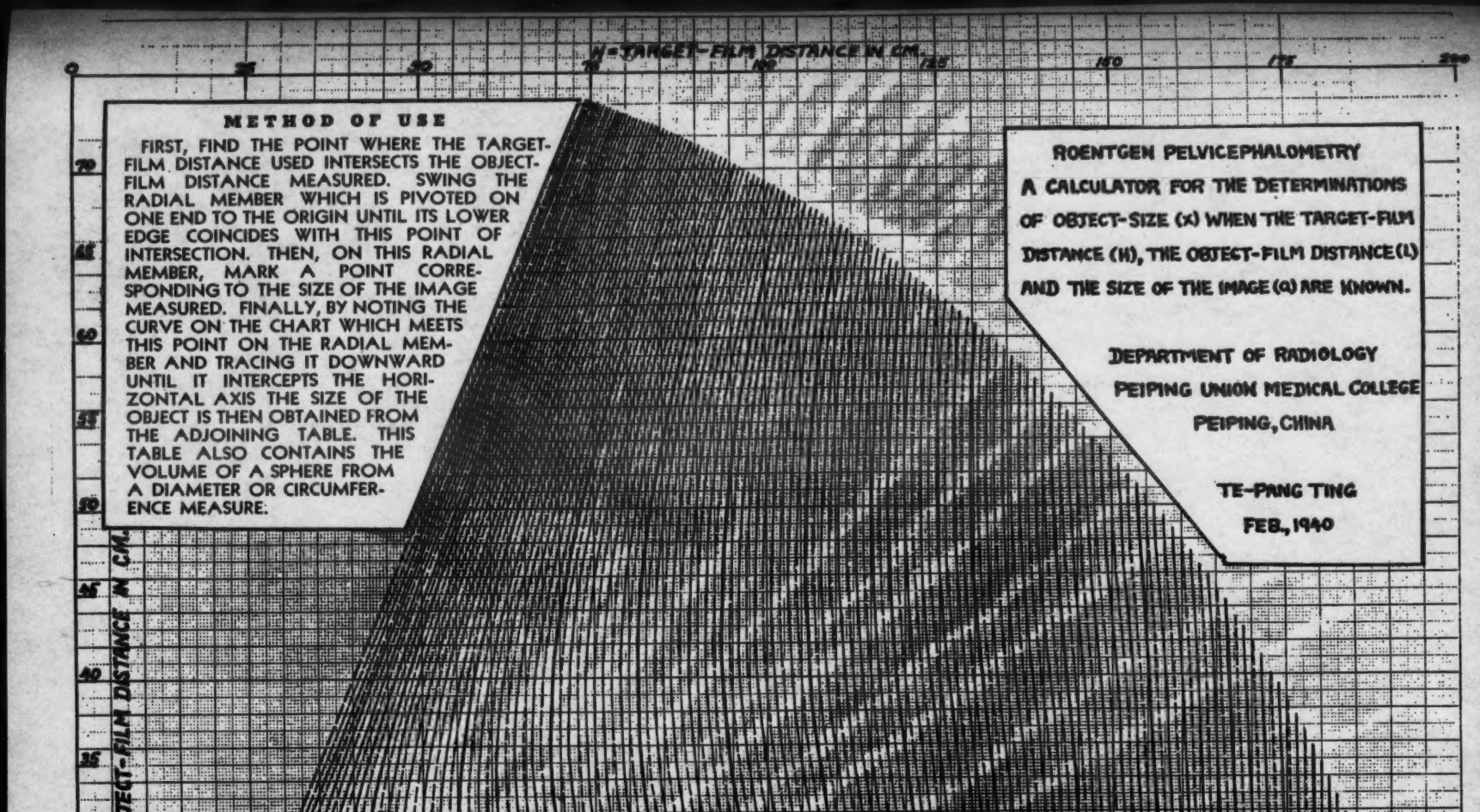
THE TRUE REPRESENTATION OF THE CHART AS A MATHEMATICAL EQUATION

The soundness of equation (1) is mathematically well established. It remains to examine how closely this chart follows the working significance of this equation.

First, by following the curve of a given object-size upward, one notices that as the polar angle is increased corresponding to an increase of the L/H ratio (either due to an increase of L or a or decrease of H, or both), the size of the image is also increased. This conclusion is in harmony with the statement that for a given size of an object, the image-size can be increased either by an increase of object-film distance or by a decrease of target-film distance or by a combination of both.

Second, if now the image-size is kept constant by marking a point on the movable radial member, one observes that as the polar angle is increased due to the

[2] For the determination of the object-film distance in pelvicephalometry refer to the articles by Ball (1) and Hodges (4).


H=TARGET-FILM DISTANCE IN CM.
100
125
150
175
200
I=OBJECT-FILM DISTANCE IN CM.
METHOD OF USE
FIRST, FIND THE POINT WHERE THE TARGET-FILM DISTANCE USED INTERSECTS THE OBJECT-FILM DISTANCE MEASURED. SWING THE RADIAL MEMBER WHICH IS PIVOTED ON ONE END TO THE ORIGIN UNTIL ITS LOWER EDGE COINCIDES WITH THIS POINT OF INTERSECTION. THEN, ON THIS RADIAL MEMBER, MARK A POINT CORRESPONDING TO THE SIZE OF THE IMAGE MEASURED. FINALLY, BY NOTING THE CURVE ON THE CHART WHICH MEETS THIS POINT ON THE RADIAL MEMBER AND TRACING IT DOWNWARD UNTIL IT INTERCEPTS THE HORIZONTAL AXIS THE SIZE OF THE OBJECT IS THEN OBTAINED FROM THE ADJOINING TABLE. THIS TABLE ALSO CONTAINS THE VOLUME OF A SPHERE FROM A DIAMETER OR CIRCUMFERENCE MEASURE.
ROENTGEN PELVICEPHALOMETRY
A CALCULATOR FOR THE DETERMINATIONS OF OBJECT-SIZE (x) WHEN THE TARGET-FILM DISTANCE (H), THE OBJECT-FILM DISTANCE (I) AND THE SIZE OF THE IMAGE (a) ARE KNOWN.
DEPARTMENT OF RADIOLOGY
PEIPING UNION MEDICAL COLLEGE
PEIPING, CHINA
TE-PANG TING
FEB., 1940

L/R=0 d=1
X=DIAMETER OR CIRCUMFERENCE IN CM.
VOLUME IN C.C. FROM DIAMETER IN CM.
VOLUME IN C.C. FROM CIRCUMFERENCE
R=IMAGE IN CM., DIAMETER OR CIRCUMF.
L=OBJECT-FIL

The Accuracy of Focal Spot Size Determination: Some Theoretical and Practical Considerations[1]

LEWIS G. JACOBS, M.D.

Indianapolis, Ind.

IN DETERMINING the size of the effective focal spot of an x-ray tube, it is a common misconception to believe that a simplified schematic consideration of the

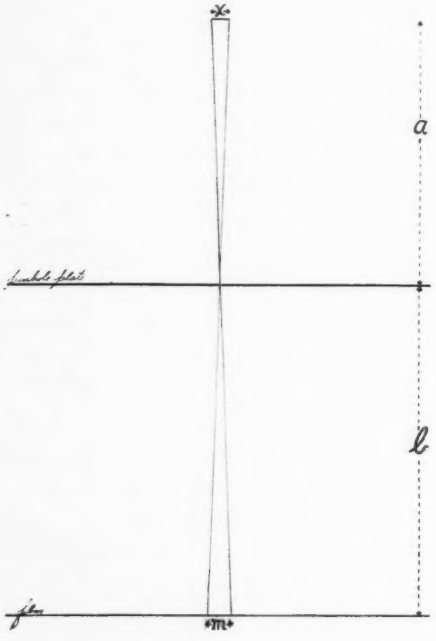


Fig. 1.

theory will lead to a reliable formula for the conversion of shadow measurements to effective projected sizes, using several known factors. But the problem is by no means so simple; the errors so introduced are very large indeed. For this reason a more complete discussion of the theory and its application is here undertaken.

If we set up the idealized arrangement commonly used (Fig. 1) with pinholes considered of zero dimension and focal spot, film, and pinholes effectively parallel, it is obvious that the ratio of the effective focal spot size in the tube to that on the film is equal to the ratio of the respective distances from the pinhole; or to put it as a formula[2]:

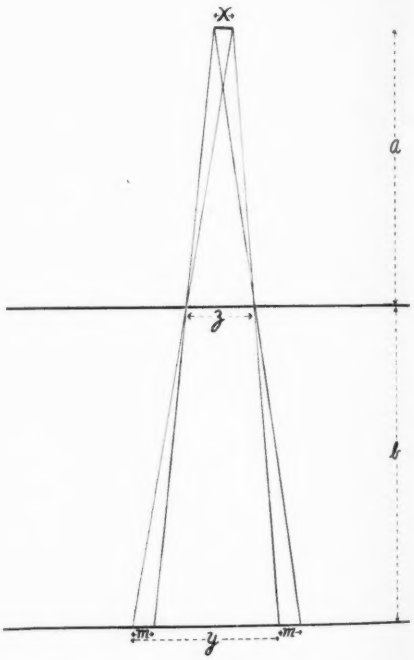


Fig. 2.

$$\frac{x}{m} = \frac{a}{b} \qquad (1)$$

Hodges (3) pointed out that if the distances a and b were unknown, a multiple pinhole arrangement would lead to a similar formula, employing the distance between pin-

[1] Presented before the Radiological Society of North America, at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

[2] Key to symbols: a. Distance from target to pinholes. b. Distance from pinholes to film. m. Size of film image of target. x. Size of projected focal spot measured in tube. y. Distance between corresponding points of the film images. z. Distance between pinholes.

holes, z, and between corresponding points of the film images, y. Hodges preferred a three pinhole system, but theoretically only two are necessary (Fig. 2). His formula, the lettering changed to correspond to our drawing, is

$$x = \frac{mz}{y - z} \tag{2}$$

Such a formula is of great utility with enclosed tube heads, which make measurement of the focal spot pinhole distance a matter of great difficulty. Both these formulae, however, are derived by assuming false conditions. The dimensions of the focal spot shadow on the film are materially affected by the size of the pinhole; while the tilt of the target face, although negligible under proper conditions, may introduce confusing differences between the size of the two shadows in the double pinhole method.

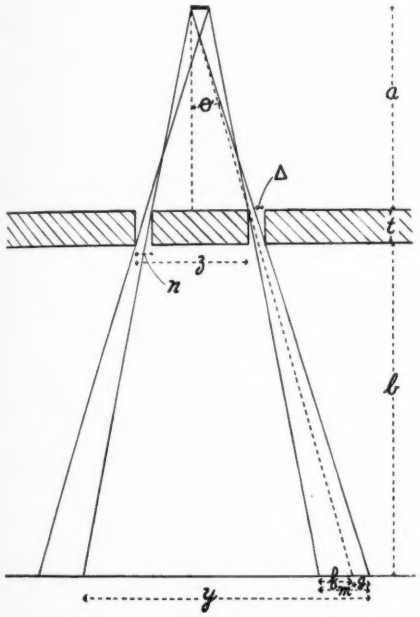


Fig. 3.

For the sake of simplicity, it is advisable to divide the problem into three parts: the effect of pinhole size; the effect of the target face tilt; the effect of inaccuracies of measurement. In order to make the division, simplified conditions are of necessity assumed, but it will be shown in each case that no significant error is thus introduced.

EFFECT OF PINHOLE SIZE

In Figure 3 we have set up an arrangement in which a pinhole of finite size is used with film, pinhole camera, and target face effectively parallel. This does not take into account the target tilt. Let us assume that our two pinholes are cylindrical, with a diameter n and a depth t (this is, of course, the thickness of the lead plate). If we make our pinholes equal in size, it makes the calculation simpler; and instead of calling z the distance between pinholes, we now define it as the distance between corresponding points of the pinholes. The values of a, b, m, x, and y remain unchanged. To derive a formula expressing x in terms of the other factors, it is first necessary to construct a line dividing m into f and g, as shown in the drawing. By similar triangles,

$$f = \frac{x}{a}(b + t) \tag{3}$$

$$g = \frac{a + b + t}{a}(n - \Delta) \tag{4}$$

$$\Delta = t.\tan\theta \tag{5}$$

$$m = f + g = \frac{x(b + t) + (a + b + t)(n - t.\tan\theta)}{a} \tag{6}$$

therefore

$$x = \frac{am - (a + b + t)(n - t.\tan\theta)}{b + t} \tag{7}$$

but

$$a + b + t = \frac{ay}{z - t.\tan\theta} \tag{8}$$

so substituting and clearing we derive

$$x = \frac{mz - ny + t.\tan\theta\,(y - m)}{y - z + t.\tan\theta} \tag{9}$$

This formula is general for the conditions assumed. It may be simplified somewhat by restricting the cases considered to two; the long axis of the tube and the line connecting the pinholes may

either coincide or be perpendicular. We may easily neglect other conditions. In the first instance, we observe that

$$\tan \theta = \frac{1/2(y + m)}{a + b + t} = \frac{1/2(z + n)}{a + t} \quad (10)$$

so that we may now state, by substitution in (4)

$$g = \frac{2n(a + b + t) - t(y + m)}{2a} \quad (11)$$

so

$$m = \frac{x(b + t) + n(a + b + t) - 1/2t\,(y + m)}{a}. \quad (12)$$

Since

$$\frac{z - \Delta}{y} = \frac{a}{a + b + t} \text{ and } \Delta = \frac{t\,(y + m)}{2(a + b + t)}, \quad (13)$$

solving and substituting in (12)

$$x = \frac{2a(mz - ny) + t(y + m)\,(z - n)}{2a(y - z) + t(y + m)} \quad (14)$$

and we have eliminated the angular measurement. But in the second instance we have an even simpler situation, since the angle θ and its tangent here are zero. Substituting this value in (9) we have

$$x = \frac{mz - ny}{y - z} \quad (15)$$

which is a very simple equation similar to that of Hodges. It contains one extra term, $-ny$; this is the correction for pinhole size. The simplicity of this formula almost demands that the axes of the pinholes and tube be perpendicular, in order to take advantage of it. Another reason for adopting this procedure will appear later.

If conditions are such as to demand formula (14), and instead (15) is used, an error will be introduced; but an estimate of the extent of this difference with figures drawn from experiment gives a value not over 1 per cent. While this might be significant in some circumstances, its importance dwindles when it is viewed beside other sources of unavoidable error to be discussed. It can be shown, moreover, that the larger a the smaller the error; thus a large value of a, the target-pinhole distance, is advantageous.

EFFECT OF TARGET FACE TILT

In Figure 4 we have a set-up for the consideration of the effect of target face tilt. Before we derive a formula, a glance will inform us of one very important fact, namely, that if the long axis of the tube

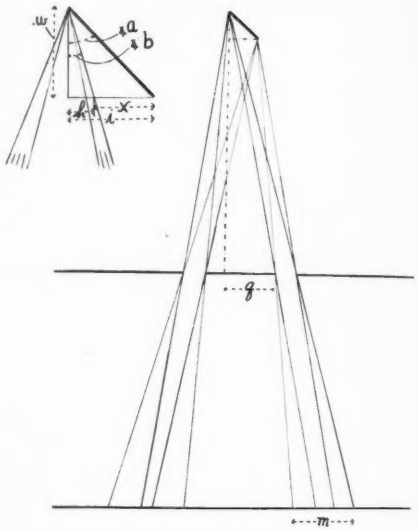


Fig. 4.

and the line between pinholes coincide, the images on the film cannot be of the same size (1, 2). The magnitude of the difference varies with the distance a, and depends on the difference in the effective size with the change in angle. Let us now take for consideration the image toward the heel of the target. If we drop a perpendicular from the toe of the target, it will intersect the plane of the pinholes at a distance q from the near edge of the "heel" pinhole. Usually this intersection will occur between the pinholes (q is less than z); but we need not assume this. By construction the angle between i and w is a right angle; so

$$x = h + i \quad (16)$$

$$\frac{h}{w} = \frac{q + n}{a + w} \quad (17)$$

but

$$w = \frac{i}{\tan \alpha} \tag{18}$$

so

$$h = \frac{i}{\tan \alpha} \cdot \frac{q+n}{a + \frac{i}{\tan \alpha}} = \frac{i(q+n)}{a.\tan \alpha + i}. \tag{19}$$

Therefore

$$x = i - \frac{i(q+n)}{a.\tan \alpha + i} \tag{20}$$

and

$$i^2 + i(a.\tan \alpha - q - n - x) - ax.\tan \alpha = 0 \tag{21}$$

While it is possible to solve this quadratic directly, we can simplify it considerably[3] by considering certain facts which limit the values of q and $\tan \alpha$. Let us assume now perfect centering of the focal spot over the pinholes, and that we have arranged the long axis of the tube parallel to the pinholes; we can see that

$$q = 1/2(z - n + x) \tag{22}$$

substituting in (21)

$$i^2 + i(a.\tan \alpha - 1/2z - 1/2n - 1\ 1/2x) - ax.\tan \alpha = 0 \tag{23}$$

But in ordinary practice, the target face takes only one of two angular values, namely, 45° or 19°, whose tangents are, respectively, 1 and 0.34433 or about 1/3. Substituting alternately these values in (23) and solving the quadratic, we find

$$\alpha = 45°,\ i = 1/4(3x + z + n - 2a + \sqrt{4a^2 - 4az + 4ax - 4an + z^2 + 6xz + 2nz + 9x^2 + 6nx + n^2}) \tag{24}$$

$$\alpha = 19°,\ i = 1/12\ (9x + 3z + 3n - 2a + \sqrt{4a^2 + 12ax - 12an + 81x^2 - 12az + 9z^2 + 54xz + 18nz + 54nx + 9n^2}) \tag{25}$$

Note that the negative value of the term under the radical has no significance, since the first set of terms is always negative. The value of i differs from that of x by about 5 per cent at 45°, or 20 per cent at 19°, as determined by these formulae, a very significant difference (see Table II). But if the axis of the tube is centered across the pinholes,

$$q = 1/2(x - n) \tag{26}$$

and again substituting this and the values of $\tan \alpha$ in equation (21) we have

$$\alpha = 45°,\ i = 1/4(3x + n - 2a + \sqrt{4a^2 + 4ax - 4an + 9x^2 + 6nx + n^2}) \tag{27}$$

$$\alpha = 19°,\ i = 1/12(9x + 3n - 2a + \sqrt{4a^2 + 12ax - 12an + 81x^2 + 54nx + 9n^2}) \tag{28}$$

These formulae are simpler and for large values of a differ by about 1 per cent at 45° and 3 per cent at 19°, an error which may be neglected under most circumstances (Table II). Thus if the tube is aligned across the line of the pinholes, no correction need be made for target tilt. We might remark here that we have always calculated the dimension in the direction of the target tilt, leaving the other to be determined by proportion; the alternate formula could, of course, also be used.

One other curious feature presents itself: if the arrangement be such that the angle α is equal to or less than β, the value of x, the apparent focal spot size, will be zero; in other words, the heel of the target cuts off the shadow of the corresponding pinhole. If there is approximate centering of the target face between the pinholes there is little likelihood of this occurring unless a is short and z is large. On the other hand, off-centering the target will produce this effect more readily. It is also noteworthy that as a increases, the value of i approaches that of x more closely. With a large value of a it is also apparent that the difference in size be-

[3] The make-up of this page has been governed by the nature of the text. Continue from this point to top of second column, to equations (24) and (25), then first and second columns to equations (27) and (28).

TABLE I: MEASUREMENTS MADE ON SEPARATE DAYS ON EACH OF SIX SHADOWS

1 First Trial	1 Second Trial	2 First Trial	2 Second Trial
6.1 × 13.0	6.2 × 13.0	6.2 × 13.0	6.1 × 12.9
6.3 × 13.3	5.9 × 13.0	6.2 × 13.1	6.2 × 12.9
6.5 × 13.0	6.1 × 13.0	6.5 × 12.8	6.1 × 12.8
6.2 × 13.1	6.1 × 12.9	6.3 × 12.9	6.2 × 12.8
5.9 × 12.9	6.3 × 13.2	6.8 × 12.9	6.4 × 13.0
6.2 × 13.1	6.2 × 13.1	6.3 × 13.1	6.3 × 12.9
6.1 × 13.2	6.2 × 13.0	6.5 × 12.8	6.3 × 12.9
6.0 × 13.0	6.0 × 12.8	6.4 × 12.8	6.1 × 12.7
6.0 × 12.9	6.2 × 12.9	6.2 × 12.8	6.4 × 13.2
6.1 × 13.2	6.1 × 13.1	6.2 × 12.9	6.3 × 12.6
Average 6.14 × 13.07	6.13 × 13.00	6.36 × 12.91	6.24 × 12.87
3	4	5	6
7.0 × 13.1	5.3 × 12.9	13.0 × 28.3	15.0 × 29.1
6.7 × 12.9	5.8 × 13.2	13.1 × 28.3	14.7 × 29.0
6.9 × 12.7	5.8 × 13.2	12.9 × 28.4	15.1 × 28.8
7.0 × 12.9	5.2 × 13.0	12.8 × 29.0	14.8 × 28.8
6.6 × 13.5	5.5 × 13.4	12.1 × 29.0	14.2 × 29.6
6.8 × 13.1	5.4 × 12.9	12.8 × 28.8	14.9 × 29.1
6.9 × 12.9	5.4 × 13.3	13.0 × 28.5	14.9 × 28.6
6.6 × 13.0	5.2 × 13.3	12.9 × 28.8	14.9 × 29.1
6.7 × 12.8	5.5 × 13.2	12.9 × 28.4	14.8 × 28.8
6.8 × 13.2	5.2 × 13.0	12.8 × 28.6	14.5 × 29.0
Average 6.80 × 13.01	5.43 × 13.14	12.83 × 28.61	14.78 × 28.99

Note that the smaller dimensions on shadows 1 and 2 are almost identical; while on shadows 3 and 4 a difference of 1.4 mm. is present. The first are a pair with the axes of the tube and pinholes perpendicular; the second a pair with these axes parallel.

tween the focal spot shadows mentioned previously is minimized. Thus we have two more reasons for keeping the focus-pinhole distance as large as possible.

Considering the evidence just presented, it would seem that the effect of target face tilt could be neglected if the tube is approximately centered with the axes of the tube and pinholes perpendicular, and if the value of a is large both in an absolute sense and with respect to the value of z.

EFFECT OF INACCURACIES OF MEASUREMENT

The critical point of the whole discussion, however, is the accuracy with which we can measure the various dimensions. Now if we use ordinary values of a and b, say in the region of 25 cm., it is quite practical to measure to about 2 per cent (5 mm.). The value of t (the plate thickness) can be measured to the nearest 0.01 mm. or 1 per cent with a micrometer. Since these three values do not appear in equation (15), errors in the measurement will not affect the result; but in the other equations, which might be of occasional interest, errors of the magnitude of 10 per cent in each of these produced errors in the result less than 1 per cent in size on several trials. We can therefore neglect the error in measuring these values. Errors in measuring m, y, and z, however, may appear in the final result as much as doubled, and errors in n may appear equal to doubled. It is quite easy to determine any of these values to the nearest 0.5 mm.; but in the case of m or n this value might well be 50 per cent of the whole size. Since the error may then pass along into the final answer doubled, it merits some attention.

To begin with, a series of actual measurements on several of the pinhole radiographs was undertaken, and the record (Table I) demonstrates that the error is substantially as stated. It also shows that an average of about ten measurements is accurate to about 0.1 mm.; which would suggest that such an average is the thing to use. We also note that the error is roughly the same in millimeters whatever the size of the shadow; so that if we make b several times a, enlarging the shadow, we can reduce the percentage of

TABLE II: VALUES OF $\frac{i-x}{x} \cdot 100$ FOR VARIOUS VALUES OF a, $z = 10$, $x = n = 1$

(This is the per cent error introduced by neglecting the target tilt)

For-mula	Angle α	$a =$ 10	$a =$ 50	$a =$ 100	$a =$ 1,000	$a =$ 10,000
24	45°	100.0	10.8	6.0	0.6	0.06
27	45°	9.9	2.0	1.0	0.1	0.01
25	19°	358.7	49.3	21.0	1.8	0.19
28	19°	27.7	6.0	3.0	0.9	0.03

Note that values of a less than 100 times the focal spot diameter give results seriously in error for the conditions assumed.

error as greatly as we please. True, we magnify the effect of any error still present somewhat when we convert by equation (15), but not enough to prevent a marked improvement in accuracy.

Measurement of the shadows under magnification, another solution of the same problem, has not proved very satisfactory; it requires special equipment, and the edges of the shadows to be studied are anything but sharp under the microscope. In a properly equipped laboratory this would furnish a satisfactory alternative method of avoiding inaccuracy if the average of a number of measurements were taken. A moderate magnification, 20 diameters or so, would appear optimum.

SUMMARY

The method of taking a pinhole camera picture may be briefly put into the following scheme:

1. Set up a plate, pinhole camera with two equal pinholes[4] (their exact size is immaterial, so long as it is known), and the tube to be tested parallel. The distance between the tube and pinholes should be fairly large, and between the pinholes and the film at least twice and preferably several times the distance between the pinholes and tube. The tube should be so oriented that the long axis is perpendicular to the line between the pinholes.

2. Make an exposure sufficiently long to give a dense black shadow of each pinhole image.

3. Examine the shadows; if they are not the same size, or if they are not so oriented that the line connecting them passes parallel to the margins, the set-up is wrong and should be adjusted properly.

4. Measure the shadow and the distance between the outside edges of the shadow ten times at intervals, and determine the respective averages for the values of m and y.

5. Substitute the appropriate values in equation (15), and determine x, the size of the effective projected focal spot.

[4] It is suggested that the pinholes be cut in a sheet of type-metal, as this is harder than lead and takes a better hole; also it is less apt to be damaged by bending.

CONCLUSIONS

From the considerations set out, it appears that formula (15) gives an accurate enough estimate of the effective projected focal spot size for clinical use without further correction, provided the tube is centered between two pinholes with its principal axis perpendicular to the line connecting the pinholes, and provided the target-pinhole distance is large both in an absolute sense and with regard to the distance between the pinholes. Inasmuch as the measurement of the shadows on the film is subject to a rather large error, it is desirable to use the average of at least ten independent measurements for the values of both shadow size and the distance between the shadows. For extremes of accuracy the method seems impractical, although it is conceivable that special camera construction might allow sufficient improvement in accuracy, particularly if extra fine grain film and extremely small pinholes were employed to diminish the penumbra.

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DISCUSSION

R. R. Newell, M.D. (San Francisco, Calif.): I am always interested in people who are hunting for errors. In the first place, I must have missed Dr. Jacobs' reason for using two pinholes. If he will answer that in his closing discussion, I shall be obliged.

In the second place, there may be two reasons why we are measuring the focal spot of an x-ray tube. First, we want to know how sharp a shadow we can get from the tube, and second, we want to know how large a load we can put on the focal spot. For either purpose what precision do we need?

As to the shadow, I have demonstrated that an unsharpness amounting to half the diameter of the shadow does not destroy the visibility. If that degree of fuzziness is tolerable, a very large error in the determination of the size of the focal spot must be tolerable.

The loading on the surface of the focal spot, as can be seen from the photographs that have been thrown on the screen, is very uneven. There are portions of the focal spot which are loaded twice as heavily as other portions. As a consequence there is a very large uncertainty in the relationship between the average loading and the maximum loading. A small error, therefore, even 10 per cent, in the determination of the total size of the focal spot must hardly be important.

My point is that the ordinary error in determination of the focal spot as brought out by Dr. Jacobs is, as far as I can see, completely within the needs of radiology.

Lewis G. Jacobs, M.D. (*closing*). In answer to Dr. Newell's question about the use of the two pinholes, the reason is simply that many tubes nowadays are enclosed in heads so that it is impractical to measure the distance between the mat and the target face.

In answer to the second point, the error may very well amount to 100 per cent in dealing with fine focal spots if a careless method of measuring the shadow is used. A 1.0 mm. focal spot shadow may be calculated 2.0 mm. in diameter if the calculation is not made in the right way, and an error of 100 per cent cannot be tolerated.

This method is not accurate to more than 5 per cent at the very best. One reason for that is, of course, that the focal spot shadow is in itself anything but sharp, and we cannot hope to make it sharp by any amount of maneuvering of the films.

The Evolution of Dosimeters in Roentgen Ray Therapy[1]

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THE FIRST ROENTGEN RAY DOSIMETER

THE FIRST estimates of quality and quantity of roentgen rays were made by observations of the density of the shadows cast by the bones and flesh of the operator's hand upon fluoroscopic screens and photographic plates (1896). The injuries which resulted from this procedure led to the use of the bones of skeleton hands imbedded in wax as a substitute for living hands. This contraption was called the "osteoscope." It was the first roentgen dosimeter.

ARITHMETIC COMPUTATION OF ROENTGEN RAY DOSE

Radiologists soon learned that the roentgen ray skin dose depended principally upon four technical factors: Voltage at the tube which was measured by inches of spark gap, current through the tube measured in milliamperes, focal skin distance in inches, and time of application. These factors then were arranged in formulae to calculate skin dosage with unfiltered and later with filtered roentgen rays for different treatment conditions (1, 2, 3). The pattern of a formula in general use was:

$$Dosage = \frac{Milliamperes \times (Spark\ Gap)^2 \times Time}{(Focal\ Skin\ Distance)^2}$$

The relative importance of these factors, however, was not well understood for many years. For example, the following statements were published as late as 1922 (3): "If you double the voltage, you double the dose, when the roentgen ray is used without filter"; and further, "filtered ray gives only double the dose at half distance instead of four times."

Even when such formulae were used correctly, they took into account only the energy put into the tube and not the quality and quantity of roentgen rays emitted. These varied considerably with different tubes and high-tension generators. For this reason the arithmetic computation of roentgen ray dosage was found to be inaccurate and the method eventually was discarded.

ROENTGEN DOSIMETRY BASED UPON CHEMICAL REACTIONS (1902)

Röntgen called attention to some of the chemical reactions created by his "new kind of ray" when he made his original reports of the discovery. Chemical reactions began to be used as methods to estimate dosage in roentgen therapy in about 1900.

In 1902 Holzknecht (4) presented his "chromoradiometer." This consisted of small discs of a fused mixture of KCl and Na_2CO_3 which became discolored when exposed to roentgen rays. He arbitrarily called a certain degree of discoloration "1 H." A light erythema skin reaction would be produced by "3 H."

In 1904, Sabouraud and Noiré (5) proposed their "radiometer," which was an improvement. This chemical method was based upon the degree of coloration of small pastilles of compressed barium platinocyanide varying from bright green ("tint A") to deep orange ("tint B"), depending upon the quantity of radiation. "Tint B" represented a full erythema dose.

Holzknecht (4), Bordier, Hampson (6), Corbett, and others devised scales to compare intermediate color changes for the estimation of fractions of erythema doses. The Holzknecht scale was divided from 0 to 8, "5 H" being made to correspond to "1 S-N" (Sabouraud-Noiré). Hampson subdivided his scale into "25 Ha," whereby

[1] Presented as an exhibit at the Twenty-sixth Annual Meeting of the Radiological Society of North America, Cleveland, Ohio, December 2–6, 1940.

"16 Ha" corresponded to "1 S-N." In all of these measurements the pastilles were placed at one-half focus skin distance to estimate the quantity of radiation. Later they were placed directly upon the skin of the patient in the field irradiated. The Sabouraud-Noiré pastilles were used in superficial roentgen therapy until recent years.

Photographic methods with paper or plates were used early to estimate dosage. A popular one was developed by Kienböck (7) in 1905. Strips of silver bromide paper were placed on the patient's skin and exposed to roentgen rays. They were then developed under specified conditions. The degree of blackening was determined by comparison with a standard scale. "Depth dose" also was estimated by this procedure by covering parts of the paper strips with different thicknesses of aluminum during exposure. The Kienböck dose unit was called the "X" and "10 X" represented an epilation dose.

Other chemical dosimeters (Freund, Glocker, Wintz) also gained favor. One of these was the "Kalomel radiometer" of Schwarz (8). This was based upon the precipitation of calomel from a solution of ammonium oxalate and bichloride of mercury when irradiated. The amount of precipitate or turbidity was ascertained by comparison with a scale divided into "4 Kaloms." It was found that "3.5 Kaloms" corresponded to "5 H."

A comparison of the different chemical dosage units follows:

Name	Unit	Distance	Epilation Dose
Holzknecht	H	Half	5
Holzknecht	H	Skin	1.25
Sabouraud-Noiré	S	Half	Tint B
Hampson	Ha	Skin	4
Kienböck	X	Skin	10
Schwarz	Kalom	Half	3.5

Chemical dosimeters were found to be unreliable. Even though dosage could be measured with fair accuracy for some conditions, the sensitivity was limited and skin reactions did not agree with the estimation of dosage for different qualities of roentgen rays.

THE FLUOROMETER AND SELENIUM CELL FOR MEASUREMENT OF DOSAGE

An improvement on the old method of estimating dosage by observing the fluoroscopic image of the hand was presented by Contremoulins (9) in 1902. He compared the intensity of fluorescence of the screen with the light from a standard incandescent lamp. In 1907 Guilleminot (10) substituted for the lamp, a radioactive salt to illuminate the screen. In 1926 Wintz and Rump (11) developed a "roentgen photometer," the principle of which was similar to Contremoulins' fluorometer. However, they improved the method of comparing the fluorescence on the screen with the standard lamp. Fluorometric dosage methods never gained much favor.

Another type of dosimeter, that became more popular, was the "Fuerstenau intensimeter" (12) presented in 1915. With it the changes in resistance of an irradiated selenium cell under the influence of roentgen rays were measured with a Wheatstone bridge circuit and a galvanometer. The galvanometer scale was calibrated in an arbitrary unit, the "F," "200 F" being equivalent to "5 H" for soft roentgen rays. The resistance changes of the selenium cells were not uniform and the cells had other disadvantages, such as "fatigue" and great dependence upon the quality of radiation. The intensimeter, although once popular, was not used after 1930.

MEASUREMENT OF ROENTGEN RAY QUALITY

Roentgen rays had been used for several years before it was recognized that quality is as important as quantity in determining dosage. With early dosimeters it was necessary to know the radiation quality in order to determine radiation quantity. More important was knowledge of measurements concerning distribution and penetration of the rays when treating diseases beneath the skin.

Investigation of quality followed two lines: consideration of the technical conditions influencing the production of the rays, and analysis of the rays after emission from the tube.

Those following the first method based quality determinations upon measurements of parallel spark gaps. Béclère in 1900 called the first spark gaps "spintermeters." In time, reliable spark gaps were developed. Other "indirect" instruments for measuring quality were the electrostatic voltmeters called "qualimeters" (Bergonié, Bauer), primary volt- or kilovoltmeters (Voltz), or special circuits connected with the secondary coil called "sklerometers" (Klingenfuss), or glow tubes (Braun).

Those who followed the second method based their investigations upon original suggestions of Röntgen. They studied and analyzed the absorption of roentgen rays in different materials, especially metals. In 1901 Benoist (13) introduced a "penetrometer" which he called the "radiochromometer." It consisted of a silver disc surrounded by a ring of aluminum arranged like a stair with 12 steps of increasing thickness. Photographically or with a fluoroscope, that aluminum step which matched the silver disc was determined and represented the radiation quality in "B." Similar penetrometers or "skiameters, or "crypto-radiometers," were designed by Walther, Wehnelt, Glocker, Meyer, Christen, and others. Some investigators expressed their absorption values in "coefficients of absorption"; others used the "half-value layer," which was suggested by Christen (14) in 1913.

BIOLOGICAL EFFECTS AS AN INDICATION OF ROENTGEN DOSAGE

Skin reactions were the first biological effects of roentgen rays that were observed. Naturally these reactions became the basis of expressing dosage and estimating it with the different types of dosimeters that were devised. For example, Holzknecht designated "5 H" measured with the Sabouraud-Noiré pastille as one erythema skin dose. Some preferred to use the epilation dose as the biological unit. Thus, a certain number of H, X, or F were specified to express the quantity of radiation that would produce the effect desired. But it was found difficult to compare skin doses measured with different dosimeters because they varied in their inherent dependence upon radiation quality. It was not until 1920 that this difficulty was overcome by the development of more reliable dosimeters and the definition of a "skin unit dose" (15).

The effects of roentgen rays upon other biological materials have been suggested as indicators of dosage. Although all of these investigations are of scientific interest, only a few have proved to be of practical importance. These include the Ascaris eggs of Holthusen (16), transplanted tumors of Russ (17) and Wood (18), Drosophila eggs used by Packard (19), tadpoles by Friedrich and Kroenig (29), and wheat seedlings by Henshaw (20).

MEASUREMENT OF THE ENERGY OF ROENTGEN RAYS

It would be desirable from both the physical and clinical point of view to be able to measure the amount of energy carried by the roentgen ray beam, and especially that amount which is absorbed in tissues in either calories or ergs.

As early as 1897, Dorn (21) used an air thermometer to measure the heat produced by the absorption of roentgen rays in metals. Similar experiments were conducted in 1900 by Rutherford and McClung (22) with a bolometer. Many other investigators have tried different methods and absorbing media (Wien, 1905; Bumstead, 1906; Adams, 1907; Boos, 1922; Grebe (23), 1924; Kulenkampff, 1926; Rump, 1927; Lauritsen, 1933). In 1927, Dauvillier (24) arrived indirectly at a figure of 30,000 ergs, absorbed radiation energy, per cubic centimeter of skin tissue layer for an erythema dose; others felt that about 200,000 ergs would be more nearly correct. At any rate, the actual amount of roentgen ray energy absorbed in media is so small that it is extremely difficult to measure it. A patient given a full course of roentgen therapy absorbs a total amount of energy equivalent to about that contained in a glassful of warm water.

IONIZING EFFECTS OF ROENTGEN RAYS

When roentgen rays traverse air, ions are liberated from the molecules, thus making the air electrically conductive. This ionizing property of the rays was discussed by Röntgen in his early publications and was destined to become the basis for measuring dosage. Many types of electrostatic and current measuring instruments were designed to determine the number of ions formed in air by roentgen rays. With these instruments it has been possible to measure relative quantities of radiation and the absorption in various media. It was not until about 1925, however, that they were more generally adopted for dosage measurements. The Dessauer electroscope is a typical example of one of the older types of ionization instruments devised (25).

DEFINITIONS OF ROENTGEN RAY DOSAGE UNITS BASED UPON IONIZATION

Villard (26) was the first to propose a unit of roentgen ray quantity based upon the ionization effect. He defined it in 1908 as that quantity of radiation "which by ionization liberates one electrostatic unit of electricity per cubic centimeter of air under normal conditions of temperature and pressure." This proposal was given little consideration at the time, although the definition of the unit is practically the same as that subsequently adopted by international agreement twenty years later.

Following Villard's suggestion, Szilard (27) in 1914 constructed a dosimeter to measure ionization, and calibrated it in "mega-mega-ions."

At about the same time Duane (28) presented his "E" as a unit of roentgen ray intensity at a meeting of the American Roentgen Ray Society in Cleveland. He took "as the unit of intensity a beam of x-rays that would produce an ionization current of one electrostatic unit in each cubic centimeter of air," under normal pressure and temperature. At the same time, Friedrich (29) defined his "e" unit, which was practically the same as that proposed by Villard.

The investigations of these prominent scientists in standardized dosimetry has been supplemented by those of Behnken, Failla, Fricke, Glasser, Holthusen, Kaye, Solomon, Taylor, and others, who eliminated discrepancies between their units by consultations and discussions.

Finally, a definition of a standard unit, the "roentgen" or "r," was accepted and adopted in 1937 at the Fifth International Congress of Radiology in Chicago. The roentgen was defined as "the quantity of x- or gamma-radiation such that the associated corpuscular emission per 0.001293 gram of air produces, in air, ions carrying 1 electrostatic unit of quantity of electricity of either sign."

STANDARD AIR IONIZATION CHAMBERS

The first large open air ionization chamber to measure ionization currents produced by roentgen rays was devised by Perrin (30) in 1896. Its practical significance was not recognized until twenty years later, when Duane (28) and Friedrich (29) used similar types of apparatus to establish their "E" and "e" dosage units. They realized that in order to measure the ionization in 1 c.c. of air correctly it should be surrounded by a large volume of air. Holthusen (31), Glasser (32), and others found that Duane's and Friedrich's first air chambers were still too small. Eventually "standard open chambers" were designed. Behnken's (33) was of the barrel type, Küstner's (34) the "Eichstandgeraet," Berg's (35) and later Neidu's the "compressed air chamber." Similar types were developed by Fricke, Glasser, and Failla (36). Taylor (37) of the National Bureau of Standards studied these different types and developed an American standard air chamber to determine the "r" and to make comparisons with the standard dosage units established in other countries. These comparisons led in 1932 to international agreement about the experimental establishment of the "roentgen."

MEASUREMENT OF ROENTGEN RAY DOSAGE WITH THIMBLE CHAMBERS

Radiologists thought that dosage could be measured with small ionization chambers on patients before they fully realized that the theoretical dosage units could be established accurately only with large air chambers. Szilard (27) had this idea in mind when he designed the first iontoquantimeter with a small chamber. This was a small cube with five lead walls and one aluminum window wall through which the rays were directed. Since most of the ionization in this chamber was caused by radiation from the metal walls, the theoretical definition of the ionization dosage units of Villard (26) and Szilard (27) could not be fulfilled experimentally. For this reason, later investigators tried to construct chambers with walls that were similar to air or tissue. Duane (28) made a chamber of carbon, but it was too large. Friedrich (29) used horn to imitate tissue. In 1925 Fricke and Glasser (38), in 1926 Glocker and Kaupp (39), and later Mayneord (40) concluded that the problem could be solved by thimble-sized ionization chambers of specific dimensions with walls of a material having the effective atomic number of atmospheric air. It has been proved that the Fricke-Glasser type of air wall thimble chamber, notably in the construction suggested by Victoreen, may be used to measure roentgen ray dosage over a wide range of qualities, as indicated by comparison with dosage measured with large standard air chambers. It has therefore been accepted generally for use in practice.

VARIOUS IONIZATION DOSIMETERS

Numerous commercial ionization dosimeters were designed, based upon the research work mentioned previously. Some of these are: universal-ionometer, Siemens and Halske, 1914; Reiniger-Gebbert-Schall iontoquantimeter, 1919; Friedrich iontoquantimeter, 1920; Dessauer-Veifa electroscope, 1921; Hammer-dosimeter, 1922; Siemens dosimeter, 1923; Standard roentgenometer, 1924; Küstner-"Eichstandgeraet," 1924; Strauss-Mekapion, 1936; Fricke-Glasser x-ray dosimeter, 1927; Siemens - "Integraldosismesser," 1930; Victoreen-condenser r-meter, 1930; Victoreen-integron, 1935.

THE CONDENSER DOSIMETER, EXTRAPOLATION CHAMBER, AND PHANTOMS

Two of the many types of dosimeters designed have special characteristics. In 1928, Glasser, Portmann and Seitz (41) presented a "condenser dosimeter" consisting of (*a*) a thimble chamber attached to a condenser and (*b*) a string electrometer. The condenser ionization chamber section first being attached to the electrometer, the instrument is charged to a known potential indicated on an illuminated scale. The ionization chamber section then may be separated from the electrometer and the chamber exposed to roentgen or radium radiation for a given time. By again uniting the two sections, the degree of discharge of the electrometer indicates the dose in "r" on the calibrated scale. Victoreen has improved the condenser r-meter and hundreds are used in practice.

In 1937 Failla (42) proposed a parallel plate chamber which he called an "extrapolation chamber." It has a lower electrode as part of a phantom and an upper electrode mounted on micrometer screws so that the spacing between the two electrodes can be varied with great accuracy. It is used to measure back-scattered radiation and tissue dosages.

Friedrich in 1918 discussed the significance of scattered radiation on the surface and depth dosages. He suggested the use of water phantoms as a substitute for the human body to measure the distribution of radiation. Since then wax, rice, and wood phantoms also have been used for this purpose.

ISODOSES

Measurements of the radiation distribution in the phantom for certain given technical conditions have been recorded in isodose charts. The first set of such

charts for roentgen rays was published by Dessauer and Vierheller in 1921. Later Bachem, Erskine, Glasser, Stenstrom, Weatherwax, and others published similar charts.

SPECTROMETERS. MEASUREMENTS OF RADIATION QUALITY

In 1912 Laue, Friedrich, and Knipping (43), then in 1914 W. H. Bragg and W. L. Bragg (44), discovered that roentgen rays can be refracted and reflected. Following this discovery many spectrographic methods were developed that have played important rôles in modern physics. Spectrometers are ideal qualimeters and quantimeters from a physical point of view, but are too difficult and impractical for radiologists to use. The Seemann (45) spectrograph is a type that has gained favor. It records photographically the wavelengths of roentgen rays and also the relative distribution of their intensity.

Radiologists, however, are interested primarily in the average quality of the roentgen ray beam used in treatment and its distribution in tissues. They therefore prefer some way of specifying quality according to absorption values. Total absorption curves in any absorbing medium can be easily made with modern ionization measuring instruments and those of constant potential apparatus have a close relationship to the spectral distribution of the radiation. Taylor (46) developed "standard absorption curves" to be used as practical "qualimeters." Absorption coefficients, effective wavelengths (Duane), average wavelengths (Mutscheller), and half-value layers (Christen) can easily be derived from such absorption measurements. The preferred way of expressing quality is according to half-value layer.

STANDARDIZATION COMMITTEE OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

During the past, when old types of dosimeters were used, committees from different radiological societies studied the problem of standardizing roentgen ray dosage and units and methods for measuring it. The difficulties which made their efforts unsuccessful have been pointed out previously in this outline on the history of dosimetry. When reliable methods for the mensuration of the ionizing effects of roentgen rays had been developed, the Radiological Society of North America realized the importance of collaboration between radiologists and physicists in arriving at uniformity in methods for determining dosage. Erskine, Ernst, and Glasser were instrumental in forming a committee on Standardization of Measurement of Radiation in 1925.

Enthusiastic co-operation by the members of this committee for fifteen years has led to satisfactory and acceptable methods for measuring and calculating roentgen ray dosage in air and tissue.

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CASE REPORTS

Diffuse Emphysema Following a Double Contrast Enema[1]

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The case to be reported presents the most unusual accident following an x-ray examination of the gastro-intestinal tract that has ever occurred in our experience. It is believed that the details may be of interest to radiologists.

Fig. 1. Roentgenogram showing presence of air in the retroperitoneal spaces.

A. Z., a white male aged fifty-eight, was referred to the X-ray Department for an examination of the gastro-intestinal tract because of some vague digestive disturbances.

The stomach showed a large deformity involving the lower half which was interpreted as due to a new growth. On the following day a barium enema revealed a poorly filled cecum. In order to determine the nature of the deformity more accurately, a contrast enema was given in the same manner as in many similar previous examinations. The air was injected by means of a Politzer bag with the patient lying on his abdomen. The nozzle was introduced by sight after being thoroughly lubricated, without undue pressure. When the injection of air was commenced a peculiar squeaking noise was heard and a great deal of resistance was experienced during the squeezing of the bulb. Since it was thought that the nozzle might be obstructed, it was withdrawn and examined for any possible obstruction of the lumen, but none was found. Neither was any blood noted upon the nozzle which might suggest traumatism to the rectal mucosa. The nozzle was carefully reintroduced with the same results as before.

Fig. 2. Roentgenogram showing air in the fascial planes of the neck and the retropharyngeal region.

When the patient began to feel fullness of the abdomen a roentgenogram was made (Fig. 1). To our great surprise instead of finding air in the bowel it was seen in the retroperitoneal spaces, especially around the kidneys. The patient was then examined in the erect position to see if there was free air in the peritoneal cavity, but none was noted. Since the patient appeared to be none the worse for his experience he was allowed to go home and advised to stay in bed. Three hours later he returned because of difficulty in swallowing and more or less labored breathing. Examination revealed marked emphysema of the neck, and a roentgenogram showed air in the fascial planes of the neck and retropharyngeal region (Fig. 2). Air was also present in the anterior mediastinum and below the diaphragm (Fig. 3), apparently between the muscle and peritoneal membrane, since no free air was found in the peritoneal cavity.

After a consultation with the surgeons it was

[1] Accepted for publication in August 1940.

decided to leave the patient alone and watch him for any possible untoward developments.

Within several days the symptoms referable to the emphysema entirely disappeared and x-ray examination failed to demonstrate any free air in the tissues. A proctoscopic examination was made in order to confirm a suspected fistulous tract which was thought to be present, but neither palpation nor inspection revealed anything unusual with the exception of internal hemorrhoids. Subsequently the patient was operated upon for the carcinoma of the stomach, which was found to be inoperable. He died a week later. No autopsy was obtained.

Fig. 3. Roentgenogram showing air in the anterior mediastinum and below the diaphragm

DISCUSSION

The question as to how the accident occurred still remains unanswered. The insertion of the nozzle was not forceful enough to penetrate the mucous membrane of the rectum, and careful examination failed to reveal anything suggestive of a fistulous tract. The presence of hemorrhoids might have weakened the mucous membrane but in that case streaks of blood should have been found on the nozzle. The fact remains that the nozzle must have reached beyond the rectal wall, permitting the air to accumulate in the retroperitoneal space surrounding the kidneys and extending upwards to the diaphragm and from that point forward to enter the retrosternal tissues and neck.

CONCLUSION

Extensive air emphysema of the soft tissues extending from the rectum to the base of the skull, infiltrating the retroperitoneal space, subdiaphragmatic region, anterior mediastinum, and paravertebral spaces of the neck, was caused by air insufflation of the rectum for contrast study. The patient completely recovered, suffering no ill effects, but died from an operation for carcinoma of the stomach.

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Schüller-Christian's Disease[1]

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F. W. MACKOY, M.D.
Milwaukee

Schüller-Christian's disease is being recognized with increasing frequency, some 150 cases having been reported up to the present time. Usually, it is a rapidly progressive, fatal disease of early childhood. It is much less common in adults. We were able to find in the literature only five reports of patients surviving the age of forty. Our case, we believe, is the sixth in this category.

Miss H. D., a forty-seven-year-old, unmarried white woman was seen by one of us (G. C. O.) Feb. 6, 1940, complaining of headache and weakness of seven months' duration. Dizziness and blurred vision were also present. A large central scotoma before the left eye had been observed for four years. Polyuria and polydipsia had been present for twenty-one years. The patient's illness began at the age of twenty-six with rapidly increasing thirst and polyuria. Three months later she suffered a nervous breakdown, and was delirious for seven weeks. Following recovery she complained of pain in the left leg because of which, in the course of a year, she was confined to the house. There was marked swelling in the region of the left hip at this time. These symptoms persisted for five or six years. Seven years after the onset, a generalized skin lesion appeared, passing through moist and scaly stages and subsiding spontaneously after a year. Nine years after the onset, recurrent swellings developed on the scalp which were painful and felt hot to the touch.

Five years later, in 1933, there gradually developed edema of the right ankle and leg. Following roentgen studies of the pelvis and right femur, the patient's physician started x-ray treatments of these areas, which were continued four years.

Diabetes insipidus had persisted unchanged since the onset. The intake ranged from four to six liters daily with a corresponding output. For years vague pain was fairly constant across the upper abdomen.

Examination revealed a well developed and well nourished woman with a somewhat pasty complexion. There were numerous irregularities in contour

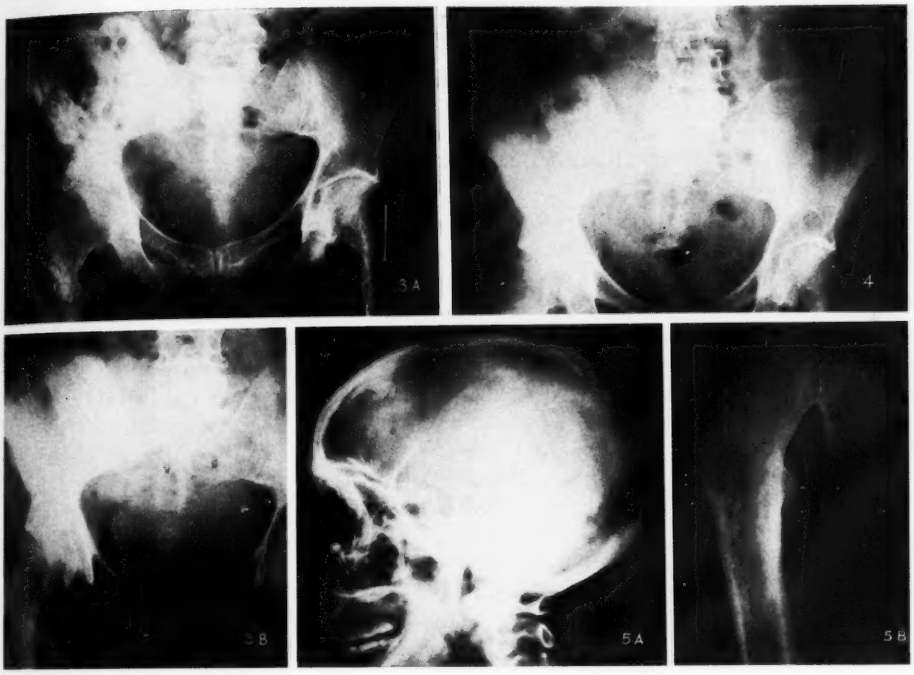
[1] Accepted for publication in August 1940.

Figs. 1–2. Schüller-Christian's disease. Fig. 1A. Skull, Sept. 21, 1925. Fig. 1B. Neck of femur, Sept. 1, 1925 (black line an artefact). Fig. 1C. Shaft of left femur, Sept. 23, 1925. Fig. 2A. Skull, July 21, 1928, showing progress of lesions. Fig. 2B. Left femur, Sept. 1, 1928, showing spontaneous healing.

of the scalp, notably over the posterior parietal regions. Examination of the eyes was negative except that the left fundus showed a sharply outlined semi-circular, slightly elevated white area, below and to the left of the nerve head and about twice its area. There was no exophthalmos. The thyroid gland was just palpable. There was no bruit. The heart was not enlarged, the rate and rhythm were normal, and there were no murmurs. The pulse rate was 84; blood pressure 186/106. The lungs were clear. The abdomen was negative, the spleen was not felt, and there was no tenderness. The right leg was edematous to the thigh. The right inguinal nodes were palpable. Laboratory studies were negative save for the low specific gravity of the urine.

The patient was placed on a low-fat, low-cholesterol diet and was given powdered posterior pituitary extract intranasally, which diminished the intake and output from six or seven liters daily to two or three liters. She lost weight on the diet and her headaches were no longer severe. While she continues to have pain in the left leg, the abdomen, and sternum, her general health is good and she is physically active.

The accompanying illustrations show the course



Figs. 3–5. Schüller-Christian's disease. Fig. 3A. Right ilium, sacrum, and femur, Sept. 23, 1933. Fig. 3B. Healing after roentgen therapy, Sept. 3, 1936. Fig. 4. Pelvis, March 4, 1937, showing increased density of bone in right ilium. Present film shows no change. Fig. 5A. Skull, Feb. 14, 1940; no roentgen therapy. Fig. 5B. Right femur, Feb. 14, 1940, after roentgen therapy.

of the bone lesions from Sept. 21, 1925, to the present time.

From June 28, 1933, until Oct. 25, 1933, the patient received a total of 3,678 r to various portals over the right pelvis and femur in doses of 350, 526 and 700 r. The factors were: 185 kv., 0.5 Cu plus 1.0 Al, 20 inches F.S.D. In 1934 three doses totaling 1,461 r were given, in 1935 three doses totaling 990 r, in 1936 one dose of 254 r, and in 1937 two doses of 254 r were given. The location and size of the portals were not specified.

Irradiation therapy to the skull has not yet been attempted, but it is doubtful that it would be of much value at the present time, at least in the old fibrosed lesions. Irradiation of the pituitary and hypothalamus with small doses might relieve the diabetes insipidus, even at this late date.

DISCUSSION

This case of Schüller-Christian's syndrome has been presented because of the rarity of descriptions of the disease in patients beyond the fourth decade. The retinal lesion is, we feel, the result of lipoid infiltration, rarely described. The roentgenographic records cover a period of fifteen years.

NOTE: We wish to express our thanks to Dr. E. F. McGrath of Appleton, Wisconsin, for the use of several films and the treatment records of the case.

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EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

Oblique Radiography of the Spine

The oblique projection in roentgenographic examination of the spine is not new but its use is not as widespread as its diagnostic value justifies. The utilization of this view will often permit direct visualization on the x-ray film of those osseous changes which are responsible for the occurrence of neurologic signs. In this sense it validates the clinical contention of their mechanical origin.

In 1931 Hubeny[1] pointed out the importance of the oblique projection of the spine in the lumbar area, and presented a technic for making the examination. He called attention particularly to the industrial compensation angle. In cases of injury to the spine he used this projection to delineate more clearly the articular facets, the lumbo-sacral articulation, the relation of the lateral processes of the 5th lumbar vertebra to the ilia, and the spinous processes of the 4th and 5th lumbar vertebrae.

The relationship of the articular facets of the lower lumbar vertebrae to lumbosacral and sciatic pain was discussed by Ghormley and Kirklin[2] in 1934. They stressed the difficulty of obtaining accurate visualization of these facets by the usual projections, especially the facets of the 5th lumbar vertebra, which are frequently set at abnormal angles. In order to obviate this difficulty, they modified the technic described in Meyer-Burgdorff's monograph and obtained projections with the pelvis turned exactly 32 degrees from the horizontal. The important points to be observed are (1) narrowing of the space between the articulating surfaces of the facets; (2) marginal hypertrophic changes about the facets; (3) fractures through the facets or vertebral arches; (4) increased radiability of the facets and supporting structures; (5) decreased radiability of these structures.

In a recent study of the articular facets in relation to low-back pain Badgley[3] gives a careful analysis of the anatomical variations found in the facets of these vertebrae. Studying 100 fifth lumbar inferior articular facets and first sacral superior articular facets, he found that 21 per cent of the sacral facets showed as much as 11 to 30 degrees increase of inclination. One out of every five specimens showed an appreciable asymmetry. Badgley describes the secondary changes caused by such anomalies with the consequent development of arthritic changes. These changes are illustrated by roentgenograms made in oblique projections.

Degeneration of the intervertebral disc with consequent narrowing of the disc space may result in changes in the relationships of the articular facets to each other and to the surrounding structures. Hadley,[4] in 1936, was one of the first to emphasize this. He stated that when this occurs in the dorsal or upper lumbar region a kyphos is produced, while in the lower lumbar region a subluxation of the apophyseal or posterior articulation occurs. Localized or referred pain in these cases may be due to (1) strain upon the ligamentous structures of the articulation, (2) a disturbance in the relationship between the articular surfaces, (3) encroachment

[1] Hubeny, M. J.: Radiology **16:** 720–724, May 1931.
[2] Ghormley, R. L., and Kirklin, B. R.: Am. J. Roentgenol. **31:** 173–176, February 1934.
[3] Badgley, C. E.: J. Bone & Joint Surg. **23:** 481–496, April 1941.
[4] Hadley, L. A.: J. Bone & Joint Surg. **18:** 428–433, April 1936.

on the intervertebral foramen causing symptoms of radiculitis, and (4), in extreme cases, actual bony impingement of the tip of the articular process upon the pedicle above or the lamina below.

In patients with obscure pain in the shoulder girdle the roentgen changes in this area may be surprisingly slight. On further study a segmental neuritis may be suggested as the underlying lesion and this naturally suggests the cervical spine as the site of the lesion. In 1937 Oppenheimer and Turner[5] called attention to this syndrome, for which they used the term discogenetic disease of the cervical spine with segmental neuritis. They called attention to the fact that the constant finding in their group of cases was definite narrowing of the corresponding intervertebral discs. Particularly did they stress the value of oblique projections of the cervical spine for demonstrating the intervertebral foramina and the articular facets.

Studying the occurrence of hypertrophic changes around the vertebrae in these cases, Oppenheimer and Turner noted that narrowing of the intervertebral spaces was associated with lipping of the adjacent bony surfaces. These changes were limited in general to the adjacent vertebrae and were most common in the lower cervical spine. With one exception no osteoarthritic changes were observed in the intervertebral joints. There was, however, an abnormal position of the facets, which had slipped past each other and more closely approached the adjacent vertebrae, in several instances being in actual contact with these vertebrae, as noted by Hadley. Oppenheimer and Turner stressed the changes which were found in the intervertebral foramina, which were demonstrable only in the oblique projections of the spine. In the areas opposite the narrowed discs the foramina were definitely narrowed and polygonal in outline. This narrowing may be bilateral or unilateral.

The main contention of these writers is that the radicular symptoms are produced by direct mechanical bony pressure upon the nerve roots, and not by arthritic changes. They believe that this pressure is produced by constriction of the intervertebral foramina secondary to narrowing of the disc. They also attempt to differentiate the clinical manifestations of this syndrome and those produced by spinal arthritis. They discuss at some length arthritic terminology and the general use of the word arthritis, which they consider inaccurate.

Roentgenologic experience in cases of segmental neuritis, particularly in the cervical area, and to a lesser extent in the lumbar area, confirms the statements of the various authors mentioned above as to the value of the oblique view in visualizing the anatomic and pathologic changes that may be a factor in producing the symptoms. These changes cannot be accurately demonstrated in the usual anteroposterior and lateral projections. In cases of obscure pain, which may be segmental in nature, and especially in those cases which show thinning of one or more of the discs, it is of the utmost importance to study the facets and intervertebral foramina by means of the oblique projection.

[5] Oppenheimer, A., and Turner, E. L.: Am. J. Roentgenol. **37:** 484–493, April 1937.

ANNOUNCEMENTS AND BOOK REVIEWS

RADIOLOGICAL SOCIETY OF NORTH AMERICA

REFRESHER COURSES

The Radiological Society of North America will present its Fourth Annual Refresher Series for Post-Graduate Instruction at the annual meeting in San Francisco, Dec. 1 to Dec. 5, 1941. The Refresher Series opens Sunday afternoon, Nov. 30, and continues during Sunday evening, with two-hour periods of instruction each day of the meeting. The courses will be given by outstanding radiologists and teachers in the various fields, from universities and the general practice of radiology.

There will be some changes in the plan of presentation of these courses as compared to previous years. No course will be repeated, and each will be of two hours' duration, with time for questions, discussions, rests, and relaxation. Each lecturer is putting forth his best efforts to present his subject in such a fashion that everyone who attends will get the most out of it. Further details will appear in the next issue of RADIOLOGY.

THE FAIRMONT HOTEL ANNUAL MEETING HEADQUARTERS

The Fairmont Hotel, which has been chosen as headquarters for the Twenty-Seventh Annual Meeting of the Radiological Society of North America, is situated on San Francisco's exclusive Nob Hill, but a few minutes from the city's finest shops, theaters, and business district, but away from the roar of downtown traffic, overlooking the skyline of cosmopolitan San Francisco, its beautiful bay, bridges, and the mountains beyond.

FAIRMONT HOTEL, SAN FRANCISCO

The Fairmont, occupying an entire city block, is especially suited to the requirements of the Radiological Society, with its large and small meeting and banquet rooms, huge auditorium, an exceptionally spacious lobby, and 15,000 square feet of space available for exhibits, without congestion or crowding. A wide price range of luxurious room accommo-

dations, cuisine from coffee shop meals to deluxe banquet service, and ample recreational facilities assure a most comfortable and enjoyable visit.

AMERICAN RADIUM SOCIETY

The American Radium Society, which held its annual meeting in Cleveland, in June, makes the following announcement of officers and committees for 1941–1942:

President: Hayes Martin, M.D., New York City.
President-Elect: William E. Costolow, M.D., Los Angeles.
1st Vice-President: J. E. Gendreau, M.D., Montreal.
2nd Vice-President: George C. Wilkins, M.D., Manchester, N. H.
Secretary: A. N. Arneson, M.D., St. Louis.
Treasurer: Charles L. Martin, M.D., Dallas.
Executive Committee: William P. Healy, M.D., New York, Chairman; Lawrence A. Pomeroy, M.D., Cleveland; Frederick W. O'Brien, M.D., Boston.
Scientific Program Committee: William E. Costolow, M.D., Los Angeles, Chairman; George T. Pack, M.D., New York; Peter A. Nelson, M.D., Chicago; Eugene T. Leddy, M.D., Rochester, Minn.
Publication Committee: Edward H. Skinner, M.D., Kansas City, Mo., Chairman; Zoe A. Johnston, M.D., Pittsburgh; Wilbur Bailey, M.D., Los Angeles.
Research and Standardization Committee: Edith A. Quimby, Sc.D., New York, Chairman; James L. Weatherwax, Philadelphia; William S. MacComb, M.D., New York.
Education and Publicity Committee: Ashley W. Oughterson, M.D., New Haven, Chairman; Leland R. Cowan, M.D., Salt Lake City; John F. Hynes, M.D., Wilmington, Del.
Janeway Lecture Committee: Douglas Quick, M.D., New York, Chairman; Edward H. Skinner, M.D., Kansas City, Mo.; Gioaochino Failla, D.Sc., New York; William P. Healy, M.D., New York; Lawrence A. Pomeroy, M.D., Cleveland; Frederick W. O'Brien, M.D., Boston.
Committee on Arrangements: John E. Wirth, M.D., Baltimore, Chairman; James G. Spackman, M.D., Wilmington, Del.; John V. Blady, M.D., Philadelphia.
Representatives on American Board of Radiology: Douglas Quick, M.D., New York; Rollin H. Stevens, M.D., Detroit; Bernard P. Widmann, M.D., Philadelphia.

INDIANA ROENTGEN SOCIETY

A meeting of the Indiana Roentgen Society was held June 1, 1941, at the Indianapolis Athletic Club. The address of the evening, on "Cystic Disease of the Lungs," was made by Dr. Leo Rigler of the University of Minnesota. Dr. Charles Wyeth of Terre Haute was elected President of the Society; Dr. Chester Stayton of Indianapolis, President-Elect; Dr. F. C. Martin of Michigan City, Vice-President; Dr. H. C. Ochsner of Indianapolis, Secretary-Treasurer.

In Memoriam

CLIFFORD RISPIN ORR, M.D.

Announcement is made of the death of Dr. Clifford Rispin Orr, of Buffalo, New York, in March. Dr. Orr was director of roentgenology at Meyer Memorial Hospital, a position which he had held for twenty-two years, and was professor of radiology in the University of Buffalo Medical College. He was a fellow of the American College of Radiology and of the American Medical Association, a diplomate of the American Board of Radiology and a member of the Radiological Society of North America, the Buffalo Radiological Society, the New York Medical Society, and the Buffalo Academy of Medicine.

WALTER R. CLEVELAND, M.D.

Dr. Walter R. Cleveland, of Evansville, Ind., died on June 10. Dr. Cleveland was a graduate of the School of Medicine of Purdue University and studied subsequently in Vienna. He was a member of the Radiological Society of North America, the American Radium Society, and the Indiana State Medical Association, and a Fellow of the American Medical Association.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as a recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

X-RAY THERAPY OF CHRONIC ARTHRITIS (Including the X-ray Diagnosis of the Disease). By KARL GOLDHAMER, M.D., Associate Roentgenologist, St. Mary's Hospital and Quincy X-ray and Radium Laboratories; Formerly Roentgenologist, University of Vienna; Honorary Member, Mississippi Valley Medical Society. With a Foreword by Harold Swanberg, B.S., M.D., F.A.C.P. A volume of 131 pages. Published by Radiologic Review Publishing Company, Quincy, Illinois, 1941. Price: $2.00.

ÜBER DIE BEDEUTUNG DER RÖNTGENUNTERSUCHUNG FÜR DIE KARDIOLOGIE. [THE VALUE OF ROENTGEN STUDIES IN CARDIOLOGY.] Special Observations on the Significance of Cardiac Enlargements. By TORFINN DENSTAD. Supplement XL of ACTA RADIOLOGICA. A Monograph containing 80 pages. Published by P. A. Norstedt & Son, Stockholm, 1941. Price: 8.00 R.M.

Book Review

FRACTURES AND OTHER BONE AND JOINT INJURIES. By R. WATSON-JONES, B.Sc., M.Ch.Orth., F.R.C.S., Civilian Consultant in Orthopedic Surgery of the Royal Air Force; Member of War Wounds Committee of Medical Research Council; Member of British Medical Association Committee on Fractures; Member of Council and Chairman of Standing Committee on Fractures, of the British Orthopedic Association; Lecturer in Orthopedic Pathology, Lecturer in Clinical Orthopedic Surgery, and Secretary of the Board of Orthopedic Studies, University of Liverpool; Neurological Surgeon to Special Head and Spinal Centre, Emergency Medical Service; Honorary Orthopedic Surgeon, Royal Liverpool United Hospital (Royal Infirmary); Visiting Surgeon, Robert Jones and Agnes Hunt Orthopedic Hospital; Consulting Orthopedic Surgeon, Royal Lancaster Infirmary, North Wales Sanatorium, Birkenhead, Hoylake, and West Kirby, Wrexham and East Denbighshire, and Garston Hospitals. Second Edition. A volume of 724 pages with 1040 illustrations. Published by The Williams & Wilkins Company, Baltimore, 1941. Price: $13.50.

This work on fractures and other bone and joint injuries brings up to date the various developments in the treatment of fractures which have come into more wide usage during the past few years. We believe it is well balanced, giving adequate emphasis to various modern methods of treatment and at the same time giving the older manipulation methods their just recognition. Such a chapter as the one on "Avascular Bone Necrosis" is an excellent example of newer and more modern concepts of bone pathology here presented in an admirable manner.

The chapter on "Low Back Pain and Sciatica" serves to illustrate the author's departure from the usual type of textbook, to make the work more useful to the surgeon interested in the treatment of fractures as well as injuries of other types. The arrangement of the text is for the most part on a regional basis and most chapters contain an adequate review of the more important injuries whether complications of fractures or not.

At times the author is a bit dogmatic in his statements about proper types of treatment and one might take exception to several statements contained in the book. His point of view is, on the whole, however, sound, and one can feel quite safe in following the programs of treatment outlined.

The book is well illustrated with excellent photographs and reproductions of roentgenograms, and neat and intelligible drawings to illustrate the more important details of fractures not shown in the usual x-ray film. Printed on excellent paper, this is a textbook of value and will be useful to everyone interested in fractures and joint injuries.

The Employment of Physicians by Hospitals: Some Legal Aspects

During the past twenty or thirty years, there have been rapid and extensive changes in the traditional functions of the hospital and its relation to the rendering of medical care by physicians to patients. The nursing home of former times has been superseded by highly organized and heavily financed hospital institutions, admitting both charity and paying patients.

A much larger proportion of sick patients are cared for in the private general hospital today than was the case a generation ago. In 1939, one patient entered a hospital in this country every 3.2 seconds.[1] The American Medical Association lists 6,226 registered hospitals, which in 1939 admitted 9,879,244 patients and recorded the births of 1,096,950 infants.[1] There are at least another thousand institutions properly classified as hospitals which are not registered by the Council on Medical Education and Hospitals of the American Medical Association. These hospitals represent a capital investment of more than 3 billion dollars.[2]

Out of every dollar spent for medical care in this country, approximately 24 cents goes to pay a hospital bill, either in private or governmental hospitals.[3] This represents a cost of about 656 million dollars per year, of which 300 million is provided by taxes, 302 million by patients' fees, and the remainder by contributions and endowments.[4] The cost of hospitalization as a result of illness is almost as high as the total cost for private physicians' services during a given year.[3]

Growth of Hospitals.—It is apparent that the hospital occupies an important rôle in the practice of modern medicine. In assuming this position, the hospital has undergone a rapid metamorphosis in its structural make-up and the position it occupies in the treatment of sickness. The earliest hospitals were usually conceived, promoted, owned, and operated by doctors. When, however, the great increase in hospitalization began, and the need for large capital investment in technical aids to the physician became necessary, the interest of agencies and citizens outside of the medical profession was enrolled. Churches, schools, and community organizations assumed the financial burden of constructing, equipping, and maintaining hospitals, made more costly by the advent of modern scientific methods.

The influence of the industrial revolution and the urbanization of our population had its effect in increasing the construction and utilization of hospitals. Many illnesses once adequately treated in the home are now referred to the hospital for the comfort of the patient and the convenience of the physician. While perhaps many of these patients could have been saved the expense of a hospital bed and just as satisfactorily treated in their homes, it is not debatable that the hospital has been an important factor in the astonishing improvement in American mortality and morbidity experience and in the rapid progress of medical science.

While this metamorphosis was taking place, the corporation became a new cynosure in American life. The successful business men who were drafted to assist in the financing and administration of new hospitals quite naturally turned to the corporate structure for the organization of the hospital. The striking result was that the hospital, which had once been a private institution operated by a physician or a group of physicians, became in a relatively short time an impersonal organization, operated on big-business lines, enclosed in the legal shell of a corporate charter and administered by a board of trustees not infrequently composed entirely of laymen. To assist the physician in the rendering of his services to patients referred to the hospital, it became uniform practice for the hospital organization to employ and make available to him the services of assisting lay and technical personnel. The corporation employed nurses, orderlies, technicians, and interns who carried out the instructions of attending physicians

[1] J. A. M. A. **144:** 1157, March 30, 1940.

[2] The Costs of Medical Care, Chicago, The University of Chicago Press, 1933, p. 17.

[3] Committee on the Costs of Medical Care: Medical Care for the American People, Chicago, The University of Chicago Press, 1932, p. 15.

[4] Christie, Arthur C.: Economic Problems of Medicine, New York, The Macmillan Co., 1935, p. 61.

and surgeons. Likewise, it purchased expensive equipment which the rapid progress in scientific medicine decreed as necessary in modern practice.

A natural result was the "closed" staff. The hospital board restricted the use of its facilities to certain appointed physicians, and only those doctors in the community holding a position on the staff were permitted to bring their patients to the hospital. This is the customary and almost universal practice of the non-governmental hospital, of which there are 3,554 in the United States.[5]

The voluntary hospital customarily assigned a certain portion of its beds for the use of indigent patients, the cost for which was borne by paying patients and income from philanthropic sources. Members of the staff provided medical services to these patients without charge, and the responsibility for a certain amount of charity work was assumed by physicians appointed to the staff.

Eleemosynary institutions maintained by local or state governments for the care of indigents were usually professionally manned by a full-time staff employed on a salary basis. Private hospitals devoting a portion of their beds to charity patients sometimes employed licensed physicians on a full-time basis to perform the bulk of the charity services.

Employment of Physicians.—Having assumed these responsibilities in medical care, it is perhaps not surprising that the hospital soon began to extend its functions, until the corporation itself was engaged in the practice of medicine. Abandoning the old concept that a hospital was a specially equipped building where doctors could treat sick people, many institutions assumed the position of a distributing medium for medical care, obscuring the traditional personal relationship between patients and doctors, and occupying a dominant rôle in the delivery of medical service.[6]

It is now widespread practice for the hospital to employ certain physicians who perform specialized professional services for pay patients who are hospitalized. Sometimes the physician employee is paid a full-time salary by the hospital corporation; sometimes he is engaged on a percentage basis, the hospital collecting the fees charged for his services and paying over an agreed percentage to him. Probably the first specialty to feel the impact of this development was anesthesiology. The great increase in surgery contemporaneous with the growth of the modern hospital resulted in the extensive employment of anesthetists by incorporated hospitals. Clinical pathology, too, felt the effects of this trend, and licensed physicians specializing in pathology were employed in large numbers of hospitals. Thus, the hospital assumed the responsibility of providing not only physical equipment to aid the attending physician or surgeon, but employed and made available to him the assistance of certain specialists whose services were required for a large portion of patients treated in the hospital.

With the spectacular advancement in the science of radiology which came in the beginning of the present century, and the extraordinarily high cost of the mechanical aids necessary in the practice of this specialty, a great many hospitals installed x-ray equipment and employed radiologists on a similar basis. More recently, physicians specializing in other branches of medicine have contracted with hospital corporations and disposed of their services on a salary or percentage basis under a full- or part-time agreement with the hospital. If it was expedient for hospitals to employ anesthetists, pathologists, and radiologists, it is not surprising that they should also employ surgeons, clinicians, obstetricians, and other specialists. There is an unmistakable trend in this direction, the full import of which has been only recently realized.

Taking cognizance of a gradual trend toward the impersonal institutionalization of medicine and the encroachment of hospitals upon the field of private medical practice, interjecting themselves between the doctor and the patient, the Judicial Council of the American Medical Association at its annual meeting in 1936 warned that,

> "It would seem that in this time of extensive changes in hospital economics the point had arrived at which further marriages between hospitals and staff physicians that make the doctor of medicine the servant of the hospital should be stopped and a series of attempts at divorce among marriages that have already taken place should be instituted. Our accepted ethical principles are adequate at the present time and hospitals would be of invaluable assistance. It is not an impossible task but will need a militant local and national ethical spirit behind it and a frowning on those individuals in the profession who on personal grounds do not object to

[5] J. A. M. A., *op. cit.*, p. 1159.

[6] See "The Modern Hospital and its Relation to the Practice of Medicine," by the author, Am. J. Roentgenol. **43:** 442, March 1940.

the gradual subjugation of the medical profession in the growth of hospital domination."[7]

The principles and ethics of good medical practice require that there be a strong personal bond between the patient and his physician—between the sick man and the one in whose healing power he has confided. Contrary to an erroneous belief by some that the modern practice of medicine is an exact science reducible to mathematics and test tubes, sickness is today more than ever recognized as having an important psychosomatic factor. This essential personal element tends to be destroyed when there is a divided loyalty on the side of the physician. The relationship toward the patient is impaired when the physician is employed by a third party, whether that third party be a corporation or an individual, especially under conditions which permit the employer to obtain a profit from the fees paid for the physician's services. This principle is succinctly stated in the code of ethics of the American Medical Association:

"It is unprofessional for a physician to dispose of his professional attainments or services to any lay body, organization, group or individual, by whatever name called, or however organized, under terms or conditions which permit a direct profit from the fees, salary, or compensation received to accrue to the lay body or individual employing him. Such a procedure is beneath the dignity of professional practice, is unfair competition with the profession at large, is harmful alike to the profession of medicine and the welfare of the people, and is against sound public policy."[8]

Legal Questions.—This new development in the practice of medicine and the new domain assumed by the incorporated hospital present certain interesting questions of law: Is an incorporated hospital which employs a physician on a salary or other stipulated compensation, the corporation itself charging and collecting fees for the physician's services, engaged in the practice of medicine? If the answer is affirmative, another question demands consideration: Is such practice lawful?

A considerable amount of loose thinking has been indulged in by some students who have essayed to discuss these questions. Somewhat typical is the statement by Michael M. Davis, Ph.D., who in a paper entitled "Do Corporations Practice Medicine?"[9] writes: "Being neither a lawyer nor a physician, I can approach this subject with the ease born of ignorance." He proceeds then to state categorically that, "The hospital corporation, if it is a corporation, is not practising medicine in a legal sense." He continues by explaining that "it is not licensed to practice. The legal responsibility remains with the physician, although the degree of legal responsibility of a corporation for profit is, as I have said, larger than that of a non-profit organization." Similarly, the *Journal of the American Hospital Association* has stated that "the laws regulating the practice of medicine by corporations do not apply and were never intended to apply to hospitals."[10] The fact is that these statements are nothing more than the expression of a wish. An examination of the question from a legal point of view and a search of the adjudicated cases establish that the law holds differently.

Master and Servant.—A corporation—and we are in this paper concerned only with incorporated hospitals, not with hospitals owned or operated by private individuals—is a creature of the law that can operate only through the principles of agency. Being an artificial legal entity, it cannot act itself, but only through others.[11]

If the physician is regarded as a servant or agent of the corporation employing him, his acts are the acts of the corporation and the corporation is to be regarded as practising medicine. On the other hand, if the physician is regarded as an independent contractor, his acts are not the acts of the corporation and the corporation is not practising medicine. This, then, is the question: Is a physician employed by a corporation the agent of that corporation?

The answers to the questions here posed lie in the law of agency. We must, therefore, turn our attention to a definition of agency and apply it to the case of a licensed physician carrying on his practice under the employment of an incorporated hospital.

There is no great difference in the legal consequences whether we define a physician employed by another as servant or agent. Agents usually create contractual relationship on behalf of the principal. Justice Holmes said:

[7] J. A. M. A. **106:** 1197, April 4, 1936.

[8] Principles of Medical Ethics, American Medical Association, 1937, Article VI, Section 4.

[9] Proceedings of the Annual Congress on Medical Education and Hospitals, 1932, American Medical Association, p. 88.

[10] *Loc. cit.*, June, 1938, p. 65.

[11] See generally, 48 Yale L. J. 346; Notes (1939) 7 Geo. Wash. L. R. 120; (1939) 37 Mich. L. R. 961; (1939) 17 N. C. L. R. 183; N. Y. & N. H. R. R. v. Schuyler, 34 N. Y. 30.

"The distinction between a servant and an agent is the distinction between *serving* and *acting for*." Professor Huffcut explains that "a servant performs operative acts not intended to induce third persons to change their legal relations."

If the parties intentionally do certain acts which have the effect of creating an agency, the relation is established, although they did not actually contemplate such a result, and even though they call the relation something else.[12] A conscious intent to create an agency is not required; agency is created by the relation of the parties. If the act inures to the benefit of the alleged principal, a presumption of agency is raised.[13]

According to the Restatement of the Law of Agency,[14] an agent is one authorized by another to act on his account and under his control. But the control is less strict than in the case of a servant, and does not include control over physical activities. The liability of a master for torts of his servant is greater than for his agent.

The Restatement is somewhat confusing in the various definitions it sets forth to differentiate between master, agent, and independent contractor. Section 23 states that "the relationship of master and servant may exist although the law required the selection of persons for the particular work to be made from a limited class irrespective of how limited the class is, and the master is subject to liability for torts committed within the scope of employment by servants selected from such a class. . . . While the physician employed by a hospital to conduct operations is not in the normal case a servant of the hospital, yet it may be found that the house physician or the interns, subject to direction as to the manner in which their work is performed, are servants of the hospital." Obviously, the Restatement is differentiating between paid and unpaid physicians in defining the master-servant relationship.

Statutory Considerations.—The question of whether a physician is an agent of the hospital which employs him on a salary was placed squarely before the United States District Court, District of Massachusetts, in *Mallory v. White, 8 Fed. Supp. 989.* Doctor Mallory was a full-time pathologist employed on a straight salary by the Boston City Hospital. He paid a Federal income tax on his salary under protest, and then instituted a suit against the local collector of internal revenue to recover the amount so paid. The question was whether or not Doctor Mallory was an officer or employee of a state or a subdivision thereof, so as to render his salary exempt from the Federal income tax. The collector of internal revenue contended that he was not an employee, but was an independent contractor whose income was therefore taxable by the Federal Government. The court found in favor of the plaintiff, however, and ruled that the trustees' right of control over Doctor Mallory's work, whether they exercised that control or not, was entirely consistent with the relation of employer and employee, and that he was therefore not an independent contractor and was not liable for Federal income tax on his salary.[15]

There are several cases holding an employed physician entitled to workmen's compensation for an injury arising out of and in the course of his employment. This conclusion could be reached only if the physician were regarded as a servant and not an independent contractor.[16]

The general rules of agency, therefore, establish the proposition that a physician-employee is agent of his employer and the employer is himself practising medicine. This is a familiar doctrine in the law of agency: *Qui facit per alium, facit per se.* The agent is the *alter ego* of the principal and the latter is estopped to deny the agency when the essentials of an agency relation exist and third parties are induced to act with reliance thereon.[17]

MAC F. CAHAL
Executive Secretary, American College of Radiology

To be continued

[12] Hughes Lumber Co. v. Madisonville Saw & Planing Mill, 4 La. App. 662; Chandler v. Kelly, 141 S. E. 389.

[13] Neibles v. Minneapolis & St. Paul Ry. Co., 33 N. W. 332.

[14] Restatement, the Law of Agency, Sec. 2, Par. 2.

[15] See Meigs v. U.S., 115 Fed. (2d) 13 (1940), where the same court reached a contrary decision, finding different circumstances from the fact that the hospital "did not have first call" on the salaried physician who was employed part-time. The differentiation is not entirely convincing.

[16] Bernstein v. Beth Israel Hosp. (N. Y.) 199 N. Y. S. 740; Arquin v. Industrial Commission (Ill.) 181 N. E. 613.

[17] Hannon v. Siegel Cooper Co., 167 N. Y. 244, 60 N. E. 597, 52 L. R. A. 429; Fields, Inc. v. Evans, 36 Ohio app. 153, 172 N. E. 702.

RADIOLOGICAL SOCIETIES IN NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying information to keep these notices accurate and up to date? Please send information to Howard P. Doub, M.D., Henry Ford Hospital, Detroit, Mich.

UNITED STATES

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Wilbur Bailey, M.D., 2007 Wilshire Blvd., Los Angeles.

Los Angeles County Medical Association, Radiological Section.—Secretary, Wilbur Bailey, M.D., 2007 Wilshire Blvd.; Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, J. Maurice Robinson, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School) and for the second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Paul R. Weeks, M.D., 520 Republic Bldg. Meets third Friday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Secretary-Treasurer, Elliott M. Hendricks, M.D., 314 Sweet Bldg., Fort Lauderdale. The next meeting will be at the time of the annual meeting of the Medical Association of Florida in the spring.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—Secretary, Chester J. Challenger, M.D., 3117 Logan Blvd. The Society meets at the Palmer House on the second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Earl E. Barth, M.D., 303 E. Chicago Ave., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Joseph C. Bell, M.D., 402 Heyburn Bldg., Louisville. Meeting annually in Louisville, third Sunday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society. Next meeting, New Orleans, April 1942.

Shreveport Radiological Club.—Secretary-Treasurer, W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, J. E. Lofstrom, M.D., St. Mary's Hospital, Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—Secretary, P. E. Hiebert, M.D., 907 North Seventh St. (Huron Bldg.), Kansas City, Kansas. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of October, January, March, and May, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, D. A. Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society.—(Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island.) *Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, L. J. Taormina, M.D., 1093 Gates Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Paul C. Swenson, M.D., Presbyterian Hospital, New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society. — Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Justin E. McCarthy, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport; The Society meets annually; time and place of next meeting will be announced later.

The Philadelphia Roentgen Ray Society.—Secretary, Barton R. Young, M.D., Temple University Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Harold W. Jacox, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Malcolm Mosteller, M.D., Columbia Hospital, Columbia. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, Franklin B. Bogart, M.D., 311 Medical Arts Bldg., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, L. W. Baird, M.D., Scott and White Hospital, Temple. Meets annually.

VIRGINIA

Virginia Radiological Society.—Secretary, Charles H. Peterson, M.D., 603 Medical Arts Bldg., Roanoke.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee, Roentgen Ray Society.—Secretary-Treasurer, Irving I. Cowan, M.D., Mount Sinai Hospital, Milwaukee. Meets monthly on first Friday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Section on Radiology, Canadian Medical Association.—Secretary, W. J. Cryderman, M.D., Medical Arts Bldg., Toronto.

Section on Radiology, Ontario Medical Association.—Secretary, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. C. Singleton, M.D., Toronto.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Multiple Calcified Cerebral Masses with Psychosis and Convulsions. F. H. Mayfield. J. Med. **21:** 485–487, January 1941.

This case report tells of a Negro of twenty-one years, who was subject to convulsions and mental disturbances. Roentgenographic examination showed calcifications in the right parietal and left occipital areas. Both calcifications were removed surgically and on pathological examination, after decalcification, were found to consist only of fibrous tissue. The exact nature of the calcifications cannot be explained. It is suggested that they may represent calcified hematomata, calcified abscesses, or purely metabolic calcifications.

JOHN MCANENY, M.D.

Otitis and Size of the Air Cell System. Marcus Diamant. Acta Radiol. **21:** 543–548, December 1940.

In order to determine if possible the relation of the size of the air cell system in the mastoid bone to otitis, the author made a study of 905 persons, of whom 585 suffered from acute or chronic otitis, while 320 were normal. The determination of the size of the air cell systems was based on roentgenograms showing the extension of the cell system in lateral projection, this having been found to be fairly representative of the volume of the cell system. The measurement of the cell system in the roentgen picture was made with a planimeter.

As thus measured the air cell system showed a normal variation from 0 to 28 or 30 sq. cm. In chronic otitis the air cell system was of small size, the average being about one-fourth that for the normal material. In no instance did it exceed 15 sq. cm., from which the author concludes that the size of the air cell system is an etiologic factor of importance in chronic otitis. Patients with acute otitis had larger cell systems than those with chronic disease but the average was less than for normal ears.

THE CHEST

Interpretation of Chest X-Ray Films. David W. Heusinkveld. Dis. of Chest **16:** 373–376, December 1940.

The interpretation of chest x-ray films is simply a process of identifying the shadows seen on the film. This demands a knowledge of normal anatomy, the pathogenesis of disease primarily or secondarily involving the chest, the dynamic forces exerted by pathological processes, and the correlation of the densities observed and the physical findings. Adequate interpretation of the chest plate, therefore, can be made only where consultation is provided between the roentgenologist and internist. WM. H. GILLENTINE, M.D.

Diagnosis of Tuberculosis, Especially of Pulmonary Tuberculosis. Hugh M. Kinghorn. J.A.M.A. **115:** 1614–1620, Nov. 9, 1940.

Examination with the aid of x-rays is the most important means at our disposal for the diagnosis of pulmonary tuberculosis, particularly in an active stage. It should not usually be difficult for the radiologist to determine the presence of tuberculosis and to tell whether it is latent or active. Knowledge of the character and location of the shadows in the lungs often makes it an easy matter to diagnose an active lung phthisis.

Brown and Sampson (Radiology **22:** 1, 1934) stated that if by the age of twenty-five there are no parenchymatous changes in the lung suggestive of phthisis, only in rare instances will a person develop pulmonary tuberculosis, and then usually only when subjected to repeated and continuous infection. No child should leave school, particularly high school, without an examination of the chest with the aid of the x-ray. This examination would probably reveal most of the persons who during the second, third, and fourth decades of life are liable to break down with clinical pulmonary tuberculosis.

A comparison of x-ray and physical findings showed that the usual site of beginning pulmonary tuberculosis of the adult type is in the upper lobe below the clavicle, and not at the very top of the lung, where clinicians had placed it. Moderately coarse moist râles at an apex were considered the only reliable data obtained on physical examination. Among 280 patients, moderately coarse râles at an apex were present in 27 per cent, while a definite parenchymatous lesion was elicited by examination with aid of the x-ray in more than 99 per cent. Of these 280 patients with minimal lesions, 277 gave definite x-ray evidence of the disease, but in only 67 were the physical signs diagnostic. Lawrason Brown studied 503 patients with only indefinite or no physical signs. X-ray examination of these showed pulmonary tuberculosis, and sooner or later, more than 84 per cent presented clear-cut clinical evidence of disease. Of 264 patients without x-ray evidence of a parenchymatous tuberculous change, in whom none of the five cardinal diagnostic criteria (tubercle bacilli, moderately coarse râles above the third rib and third dorsal spine, a parenchymatous lesion in the same area on roentgen examination, hemoptysis, and pleurisy with effusion) was present, only two had developed lung tuberculosis after one to seven years. One of these two patients had tuberculous cervical adenitis and the other had a carious rib. Another study of 2,600 consecutive patients showed 298 with negative x-ray examinations, and of these only 2 developed tuberculosis and died of the disease. Another study was made on 312 patients who had one or more of the four cardinal diagnostic criteria and no definite x-ray evidence of tuberculosis. Of these 312 patients, only 2 died of pulmonary tuberculosis. Determination of clinical activity was possible by examination with the aid of the roentgen ray.

C. G. SUTHERLAND, M.D.

Accuracy of Fluoroscopy in the Detection of Pulmonary Tuberculosis. Harold L. Israel and H. W. Hetherington. Am. J. M. Sc. **201:** 224–232, February 1941.

In order to determine the accuracy of fluoroscopy in the detection of pulmonary tuberculosis, duplicate fluoroscopic and radiographic examinations were made in 1,021 contact cases. Eighteen physicians, with varying degrees of skill and training, participated.

The percentage of accuracy in the detection of active parenchymal lesions for the whole group of examiners was 96.6 per cent, the range being from 95 to 99 per cent. Small lesions of questionable clinical significance, but of importance in epidemiologic investigations, were frequently overlooked by physicians without special training in roentgenologic interpretation. Results satisfactory for clinical purposes were obtained even in obese patients. An especially high degree of accuracy was obtained in the fluoroscopic examination of children.

There was a fairly close correspondence between the methods of examination in the diagnosis of tracheobronchial lymph node enlargement.

The considerable divergence of the duplicate examinations in the detection of primary calcified tuberculosis

may be due to the fact that no oblique roentgenograms were made, while fluoroscopically the patient could be examined from many angles.

Since no significant abnormalities were found in testing the physicians for dark adaptation, it may be concluded that the failure to wait for adequate adaptation may account for the inaccuracies, rather than lack of training or the limitations of fluoroscopy.

BENJAMIN COPLEMAN, M.D.

Routine Chest Roentgenograms in Pregnancy: A Study Based on 800 Consecutive Cases. Hervey K. Graham. West. J. Surg. **49:** 107–112, February 1941.

The author studied routine chest roentgenograms in a series of 800 obstetrical cases in private practice. Fifty-five per cent showed normal chests. Forty per cent showed evidence of repeated respiratory infections, old pleurisy, or tuberculous contact not considered of clinical significance. Three per cent showed evidence of parenchymatous disease of the lungs which is prone to break down during pregnancy and delivery, thereby permitting prophylactic treatment and preventing activation of the disease. In one per cent of this group active tuberculosis was found. These figures compare favorably with those in mass surveys made among the poorer class of patients who report to the general clinics, and they are therefore doubly significant.

WM. H. GILLENTINE, M.D.

Indications for Surgery in Pulmonary Tuberculosis. Ross Robertson. Canad. M. A. J. **44:** 107–113, February 1941.

The author reviews the literature briefly, giving mortality and morbidity statistics which greatly favor surgical interference in selected cases of pulmonary tuberculosis.

Collapse therapy is indicated for tuberculous cavities or areas of caseation. The various types of operation are described, with their applications in particular cases. At the present time, in the Muskoka Hospital, Ontario, 53.2 per cent of patients who have been in residence for over a year have had one or more surgical operations. The most favorable time for surgical collapse is when the acute exudative disease has been followed by attempted healing by fibrosis. If patients have open cavities and large quantities of bacilli-laden sputum, the risk of waiting for the acute phase to subside may be greater than the risk of immediate operation.

Phrenic paralysis is indicated in obliterating pneumothorax or when pneumothorax is being discontinued, in the presence of cavities at the base or hilus of the lung, as an adjunct to pneumothorax or a preliminary to thoracoplasty, in hemoptysis, in pain or cough from diaphragmatic adhesions, and in minimal disease at the apex. Phrenic paralysis preliminary to thoracoplasty must always be temporary. If the diaphragm is paralyzed, atelectasis of the lower lobe may develop.

At the first operation the phrenic nerve is usually crushed, causing a paralysis of the diaphragm lasting for about six months. If results are notably successful, the nerve may be avulsed at a subsequent operation and a permanent paralysis obtained. Histories of two patients are given. The first had advanced pulmonary tuberculosis with a large cavity in the hilus of the right lung, widespread infiltration throughout both lungs, and positive sputum. The right phrenic nerve was crushed. The cavity closed and the sputum became negative. The results were so good it was decided to make the paralysis permanent. The patient's general health improved and the sputum remained negative. The second patient had a rapidly obliterating right pneumothorax. Since the right lung did not appear entirely healed the right phrenic nerve was crushed to provide additional relaxation.

Adhesions between the diseased lobe and the parietal pleura often render an artificial pneumothorax inefficient. In such cases the adhesions can be divided safely by an electric cautery and a satisfactory collapse produced. The history of a patient having bilateral pneumolysis is given.

If the visceral and parietal layers of pleura are adherent, intrapleural pneumothorax is impossible. The parietal pleura may be stripped from the chest wall and upper mediastinum. Contraindications are the presence of a large superficial cavity and inflammatory tissue. Two cases successfully treated are described.

Space in extrapleural pneumothorax may be preserved if necessary by filling it with wax. In the example cited there were no complications attributable to the wax.

The standard thoracoplasty consists in the removal of eight to ten ribs from the transverse processes to the costal cartilages of the first few ribs, grading off below. This type is used for tuberculous disease affecting most of the upper lobe. The Semb type of thoracoplasty, which is described, is indicated for disease in the extreme apex. The ideal case for thoracoplasty is unilateral disease of less than two years' duration. It has been the author's experience that thoracoplasty is of little benefit to patients who show no roentgen evidence of cavity in the lung. Patients selected for thoracoplasty must be fully grown, or a severe deforming scoliosis will result. Thoracoplasty and partial scapulectomy, anterior thoracoplasty, complete thoracoplasty including anterior stage and muscle-splitting thoracoplasty, are described.

Since surgical treatment provides collapse therapy but does not remove tuberculous tissue, the continuation of strict bed-rest after operation is essential.

Two pages of chest roentgenograms before and after surgery are included. M. L. CONNELLY, M.D.

Tracheobronchiectasis and the Factors Which Lead to Bronchiectasis. M. Kartagener and K. Ulrich. Schweiz. med. Wchnschr. **70:** 1266–1270, Dec. 28, 1940.

This report deals with a patient showing a combination of bronchiectasis and diffuse dilatation of the trachea. During the course of his military service he contracted pneumonia, after which the symptoms of bronchiectasis appeared. Diagnosis was confirmed by iodized oil bronchograms and by tracheobronchoscopy.

The authors believe that this condition is due to a congenital weakness of the tracheal and bronchial walls produced by a thinning of the muscularis and loss of the longitudinal elastic fibers, and support their opinion by a review of the literature. While atrophy may play a rôle in the aged, the evidence points strongly to a congenital origin in the case recorded, and the suggestion is advanced that all bronchiectasis may be congenital in origin.

As this case came up for a determination as to further military service and compensation, these phases are rather fully discussed. The opinion of the authors is that the pneumonia had at most only hastened an inevitable chain of symptoms.

LEWIS G. JACOBS, M.D.

Tularemic Pneumonia, Its Recognition and Prevention. Harry B. Thomas. Pennyslvania M. J. **44:** 151–156, November 1940.

The causative organism of tularemic pneumonia is the *Bacterium tularense*. Over twenty species of wild life may transmit it to man, but rabbits are the source of infection in more than 90 per cent of the cases reported. In Pennsylvania the disease was first reported in 1928, and each year an increasing number of cases have been seen, the total to June 1, 1940, being 219.

A primary lesion develops, as a rule, at the site of

inoculation, and leaves a punched-out ulcer with a necrotic floor. Regional lymph nodes are usually involved, and the infection extends along the deep lymph channels. Lung involvement is present in 90 per cent of cases, and may be clinically demonstrated in 50 per cent; definite pneumonic consolidation is seen in 18 per cent.

X-ray findings may simulate miliary tuberculosis or may suggest bronchial or lobar pneumonia or a solitary lung abscess. In later stages multiple cavitation may be seen. Pleural effusion appears in 15 per cent of cases. The diagnosis may be verified by finding the organism in the primary lesion, by blood cultures, and by skin tests.

General supportive treatment should be instituted as for any pneumonia. Foshay's antiserum produces a high percentage of severe reactions and is not of established value. The use of human immune serum and drugs of the sulfanilamide group have proved to be of no value. JOSEPH T. DANZER, M.D.

Pulmonary Infarction as a Cause of Pneumothorax. J. H. Marks. New England J. Med. **223:** 934–936, Dec. 5, 1940.

Among the causes usually given for spontaneous pneumothorax are tuberculosis, rupture of an emphysematous bleb, and the breaking down of a septic pulmonary infarct. An infarct is a manifestation of inflammation elsewhere, and when a pneumothorax or pyopneumo thorax occurs, pulmonary infarction must be considered as a possible cause.

Two case reports are presented which demonstrate the occurrence of pneumothorax after pulmonary infarction. JOHN MCANENY, M.D.

Case of Pulmonary Concussion Due to High Explosive. Geoffrey Hadfield and Ronald V. Christie. Brit. M. J. **1:** 77–78, Jan. 18, 1941.

The authors describe a case of pulmonary hemorrhage caused by bomb concussion. The clinical picture is described and the x-ray findings are referred to as a diffuse "woolly mottling" throughout the left lung. Death occurred after apparent recovery from the initial shock. Autopsy showed many areas of hemorrhagic consolidation. It was apparent that the hemorrhage was progressive and that death was hastened if not caused by transporting the patient before he had completely recovered. Q. B. CORAY, M.D.

Scleroderma with Pulmonary Fibrosis. John R. Murphy, Philip Krainin, and Martin J. Gerson. J. A. M. A. **116:** 499–501, Feb. 8, 1941.

The pathologic changes in diffuse scleroderma are not confined to skin and subcutaneous tissue but involve the connective-tissue system throughout the body. Muscle, fascia, tendon, bone, and at times even the endocrine glands and the internal organs participate in the disease process. Everywhere the same changes occur, namely, edema followed by sclerosis of the collagenous bundles.

A case is reported in which pulmonary manifestations of the disease were visualized by roentgenographic study. It was demonstrated by the induction of pneumothorax on one side that the shadow of the fibrosis was not superimposed by involvement of extrathoracic tissues. A search of the literature revealed no similar case. C. G. SUTHERLAND, M.D.

Aneurysm of the Ventricle of the Heart. Marshall N. Fulton. J. A. M. A. **116:** 115–122, January 1941.

Among the less common end-results of infarct of the heart is the formation of ventricular aneurysm. Aneurysm of the ventricle may occur, also, from abscess of the heart wall, from trauma, from ulcerative lesions of bacterial endocarditis, and from congenital defects. The majority of ventricular aneurysms arise as a result of infarction following coronary thrombosis.

The roentgenologist has made possible the accurate recognition of ventricular aneurysm during life. On roentgen examination cardiac enlargement is nearly always present; an abnormal contour of the heart with sharply defined ledging of the ventricular border is a characteristic feature. On roentgenoscopy localized aneurysms may show a paradoxical type of pulsation, expanding outwardly as the ventricle contracts. A greatly diminished or feeble beat may be observed in larger aneurysms or in those filled with a blood clot. Apical aneurysms may be difficult to visualize because the bulge may be obscured by the shadow of the diaphragm. Calcification within the wall of the aneurysm or in the clot which it contains may be of diagnostic aid.

A localized syphilitic lesion of the heart wall may simulate aneurysm. In such cases antisyphilitic therapy may lead to great improvement. C. G. SUTHERLAND, M.D.

Roentgen Kymography in the Study of the Heart in Childhood. J. Victor Greenebaum, Samuel Brown, and Theodore Selkirk. Ohio State M.J. **36:** 1194–1197, November 1940.

The authors made a survey of a group of normal children and more than one hundred children with various types of cardiac disease. The technic could not be used on infants or small non-co-operative children. Apart from an increased heart rate in the children, the study showed the same changes in the different valvular lesions as in adults. An interesting case of right-sided aorta is presented. SIMON POLLACK, M.D.

THE DIGESTIVE TRACT

Influence of Reciprocal Topographic-Anatomic Relations of the Pyloric Antrum, Pylorus, and Duodenum, on the Roentgen Picture in Different Exposures. E. Walder. Schweiz. med. Wchnschr. **70:** 1123–1128, Nov. 23, 1940.

The author proves by study of a schematic plan of the antrum, pylorus, and cap that a conical cap, seen at various angles and more or less foreshortened, will produce all the common types of bulb shadow seen. The various walls may be brought out by projections at different angles. Thus an ulcer crater may be demonstrated *en face* or *en profil* by appropriate angulation of the patient. LEWIS G. JACOBS, M.D.

Etiology and Diagnosis of Massive Hematemesis and Melena. S. Goodman. J. Med. **21:** 443–450, December 1940.

Goodman made a study to determine the cause of massive hematemesis and melena, as complained of by 329 patients. Peptic ulcer is the most frequent cause, accounting for 40.4 per cent of the series. The next largest group, 29.5 per cent, was of undetermined cause. Hepatic cirrhosis was present in 16.5 per cent and gastric carcinoma in 9.1 per cent. The remaining cases constitute a miscellaneous group, consisting of sarcoma of the stomach, dissecting aortic aneurysm, mesenteric venous thrombosis, carcinoma of the gallbladder, acute esophagitis, abdominal trauma, subacute bacterial endocarditis, thrombocytopenic purpura, saccular aortic aneurysm, gastric neuroma, carcinoma of the pancreas eroding the duodenum, retroperitoneal sarcoma, and gastric lymphoblastoma.

The incidence of hemorrhage is highest in the fourth to sixth decades; it is three times as frequent in men as in women. JOHN MCANENY, M.D.

Recurrent Peptic Ulcer: Situation of Recurrences and Importance of Studies of Pain in Recognition of Such Recurrences. Andrew B. Rivers and John W. Gardner. J.A.M.A. **115:** 1779–1785, Nov. 23, 1940.

This study included 65 cases of postoperative recurring ulcerations. The exact situation of both primary and secondary lesions was ascertained roentgenographically. The situation of the secondary ulcerations was confirmed by direct inspection of the tissues at operation. Only those cases were accepted for study which had a history that included exact information regarding the syndrome under consideration. An inquiry was made as to the situation, duration, and character of the pain, the time of its onset, and the mode of relief. A special attempt was made to compare the characteristics of the original lesion with those of the one which developed postoperatively.

The situation of the majority of recurring peptic ulcerations is in or near the site of the surgical anastomosis where operation has been performed. The physical factor probably determines the site at which the ulcer will develop. The symptoms of the recurring lesion are in general similar to those produced by the original ulcer. A majority of secondary ulcerations, however, tend to penetrate deeply and, therefore, produce symptoms which are less intermittent, cause more distress at night, and are less easily relieved by food and alkali. A great number of recurring lesions involve the site of surgical anastomosis with the production of more or less obstruction, which tends to distort somewhat the usual syndrome for ulcer.

C. G. SUTHERLAND, M.D.

Early Diagnosis and Prognosis of Gastric Carcinoma. Rudolf Schindler. J.A.M.A. **115:** 1693–1699, Nov. 16, 1940.

According to the author's studies, the polypoid carcinoma constitutes 2.9 per cent of all gastric carcinomas; an ulcer surrounded by an elevated wall is seen in 17.6 per cent; an ulcer walled off on only one side occurs in 16.3 per cent; a diffuse infiltrating type is present in 63.2 per cent, with no sharp limit anywhere toward the normal gastric mucosa either visible to the eye or demonstrable by palpation. Within the area of infiltration, ulceration—shallow or deep—may develop. The polypoid carcinoma, if operated on radically in an early stage, offers a good prognosis. The outlook in the infiltrating type is most unfavorable.

The only hope of cure lies in the recognition of the lesion in the precancerous stage. Peptic ulceration of carcinoma may produce a lesion grossly indistinguishable from benign ulcer. Polyps associated with atrophic and hyperplastic gastritis are potentially malignant. The author believes that gastric carcinoma develops on the soil of atrophic gastritis. By routine x-ray and gastroscopic examination early carcinomas of minimal size can be discovered and early surgery will obtain a higher percentage of real cures and a greater prolongation of life.

C. G. SUTHERLAND, M.D.

Gastro-Colic and Gastro-Jejuno-Colic Fistula (Report of Five Cases). E. R. Williams. Brit. J. Radiol. **14:** 36–40, January 1941.

Gastro-colic and gastro-jejuno-colic fistulae are usually discovered by barium enema rather than by barium meal. Great care is required to show the tract, as it is apt to be concealed. Expiratory rather than inspiratory films are apt to be helpful. Five cases are reported. SYDNEY J. HAWLEY, M.D.

X-Ray Diagnosis of Acute Intestinal Obstruction. P. B. Ascroft and E. Samuel. Brit. J. Radiol. **14:** 11–22, January 1941.

In the diagnosis of acute intestinal obstruction two films of the abdomen are used, one in the erect and one in the supine position. The presence of obstruction is indicated by distention of the bowel and the presence of fluid levels. Enemas should not be given prior to the x-ray examination, as false fluid levels may be produced. The loops of distended bowel are measured and the degree of distention graded, one to four, grade one representing the least amount of distention. The number of fluid levels and the degree of distention run parallel. Serious disproportion between the two suggests complications. It is usually possible to locate the obstruction. The correct diagnosis was made in 30 cases of serious obstruction. A correct negative diagnosis was made in 22 out of 27 cases. Colonic obstruction was accurately diagnosed and located in 16 out of 19 cases. SYDNEY J. HAWLEY, M.D.

Intubation Management of Distention in Intestinal Obstruction. Louis C. Bennett. West. J. Surg. **49:** 71–76, February 1941.

Since Wangensteen and Rea demonstrated the importance of the distention factor in intestinal obstruction, the use of the Miller-Abbot double lumen tube has materially reduced the mortality and morbidity of non-strangulating types of obstruction, although it will never replace the surgical management of this condition. The greatest difficulty in the use of this tube arises from the inherent impossibility of definitely differentiating the organic from the functional type of obstruction. The tube also has a definite use in the preoperative and postoperative management of obstructive lesions. One point made by the author needs even greater emphasis, "Not only must one have an understanding of the various methods employed but he must be prepared to spend the time necessary for careful and patient supervision of the entire procedure."

WM. H. GILLENTINE, M.D.

Primary Adenocarcinoma of the Jejunum. E. L. Hunt and G. D. Kaneb. New England J. Med. **224:** 353–357, Feb. 27, 1941.

Primary carcinoma of the jejunum comprises about 1 per cent of cancers of the bowel. The operative mortality is estimated by various observers to lie between 20 and 47 per cent.

Three cases are here recorded with survival eleven, eight, and two years after operation. All three patients complained of "indigestion." This may take the form of cramps about the navel, associated with borborygmus, vomiting, or salivation. Hemorrhage of variable amount may occur. Loss of weight and anemia may be early findings. X-ray studies may reveal retardation of the passage of barium and dilatation of the jejunum (or duodenum) above the lesion; the dilated portion is identified as the jejunum by its deep circumferential folds (Kerkring's). Flat films for gas reveal the typical ladder pattern according to the degree and site of the obstruction.

One patient of this group, a man of seventy-six, died after two years showing metastasis to the left femur, which was painful and unrelieved by irradiation.

Recent advances in surgical technic and preoperative and postoperative care are briefly discussed.

JOHN MCANENY, M.D.

Regional Ileitis. Wilfrid L. Graham. Canad. M. A. J. **44:** 168–171, February 1941.

The author reports 35 cases of regional ileitis treated in the Vancouver General Hospital in 1937, 1938, and 1939. The terminal ileum was involved in 34 cases, the mid jejunum in 1. The ratio of males to females was 2 to 1, with no age-group preponderance.

In 28 of the 35 cases an exploratory operation was done. Six cases were diagnosed clinically with roentgen confirmation and 1 at autopsy. The surgical cases are

grouped as follows: terminal ileitis with chronic appendicitis, 24; with acute appendicitis, 2; with complete obstruction, 2; tuberculous ileitis with no involvement of the cecum, 1. No deaths occurred in cases without involvement of the appendix.

The roentgen diagnosis was usually based on one or more of the following findings: (1) a narrowed, rigid lumen; (2) dilatation and delay above area of constriction; (3) the so-called "string sign;" (4) retention of barium at ileocecal valve after evacuation of the barium enema, best demonstrated by air insufflation.

The cause of the disease is obscure. The author noted that the portion of the bowel involved received its blood supply from the iliac branch of the ileocolic vessels. The diagnosis of terminal ileitis is not easy; 68 per cent of the cases were diagnosed preoperatively as acute appendicitis. Pain was present in all cases, nausea with vomiting in 50 per cent. Temperature range was from normal to 102°. The leukocyte count was elevated in practically every instance.

The author recommends conservative treatment in the acute stage. If diagnosis is in doubt, an exploratory laparotomy is indicated. In the chronic stage the operation of election is a wide resection of the involved bowel. Specific therapy, such as sulfanilamide or sulfapyridine, used in 5 cases, was not considered a factor in recovery. Twenty-eight of the 33 surviving patients replied to the author's questionnaire. Of these, 26 had been perfectly well, while 2 complained of residual symptoms not severe enough to interfere with their activities.

M. L. CONNELLY, M.D.

Carcinoma of the Colon: Early Diagnosis with Double Contrast Enema. J. Gershon-Cohen and Harry Shay. Pennsylvania M. J. **44:** 462–466, January 1941.

The simple barium enema fails in less than 10 per cent of cases in establishing a diagnosis of carcinoma of the colon once the patient has developed symptoms. Many of these lesions can be discovered by the use of a contrast enema and the authors state that out of 500 cases 7 lesions were found by this method that could not be seen in any other way. As one-half the patients operated on for carcinoma of the colon are already incurable, the importance of early diagnosis is obvious.

Medullary cancers grow into the lumen of the bowel and are more readily discernible. Scirrhous infiltrations are less easily seen and films taken after evacuation and double exposure are an aid in studying the mucosal pattern.

The double contrast enema is useful in revealing slight intraluminal changes, small carcinomas, and polyps, which "are nicely illuminated by the thin coating of residual barium in the air column of the double contrast enema." It has also been useful in showing the proximal loop where, because of obstruction, barium cannot pass, and it has decreased the percentage of non-visualized lesions in the rectum.

The double contrast enema calls for a three-stage examination. First, an ordinary enema, using barium in a water suspension, is given under fluoroscopic and roentgenographic control. The enema is expelled and the patient is then examined fluoroscopically and, if necessary, films are taken. After this, air is slowly injected, care being taken not to give a sufficient quantity to fill the terminal ileum.

The authors recommend the routine use of the procedure as a check on the ordinary barium enema.

JOSEPH T. DANZER, M.D.

Exploration of the Common Bile Duct for Stone. Drainage with T-Tube and Cholangiography. Michael J. Smyth. Brit. M. J. **1:** 111–114, Jan. 25, 1941.

This article is an effective exposition on the subject of cholangiography. The author calls attention to the frequent dissatisfaction following cholecystectomy, as a result of impaired function of the common duct. The symptoms of this complication are discussed.

In performing cholangiography lipiodol and thorotrast were first used, but both were finally discarded in favor of a solution called perabrodil. The examination may be made through a T-tube left in the duct or it may be done on the operating table. Methods of flushing the duct by administration of amyl nitrite or nitroglycerine are referred to and a trial of this maneuver is recommended.

The time for removal of the T-tube is said to be determined by the condition of the bile. When the bile salt content has returned to normal this may properly be done.

Q. B. CORAY, M.D.

Radiographic Findings in Two Unusual Cases of Inguinal Hernia. E. R. Williams. Brit. J. Radiol. **14:** 41–42, January 1941.

Two cases of inguinal hernia are reported. In one the appendix was demonstrated in the hernia and in the other a large loop of sigmoid.

SYDNEY J. HAWLEY, M.D.

THE GENITO-URINARY TRACT

Subcutaneous Urography. Jacob H. Vastine, Jr., and D. Alan Sampson. Pennsylvania M. J. **44:** 606–611, February 1941.

Excretion urography is a much less formidable procedure than retrograde pyelography, particularly in children. If difficulty is encountered in intravenous urography, the urographic medium may be given subcutaneously or intramuscularly. This procedure is not new; it was used as early as 1931 in Europe and in 1934 in America. It is, however, not well known and has not been used to any great extent by urologists or radiologists, who are unfamiliar either with the technic or its results.

The author uses diodrast, making a preliminary test to guard against unfavorable reactions. Adults are first given 2.0 c.c. to hold in the mouth for ten minutes, after which it is swallowed. If the cheeks and tongue do not become numb and no outward symptoms appear, the procedure is continued. In children the mouth is swabbed with the solution and possible signs of reaction are observed.

Two hypodermoclysis needles are inserted subcutaneously in the region of the angle of each scapula and 80 c.c. of saline are injected, to which have been added 20 c.c. of 35 per cent diodrast. Films are taken every five or ten minutes and the whole procedure is over in about fifty minutes from the completion of injection.

The shadows are not quite as dense as those produced by the retrograde method but appear to be fully as satisfactory as those obtained by intravenous administration. The author says, "In short, the method is satisfactory."

JOSEPH T. DANZER, M.D.

Shortcomings of Intravenous Urography. David M. Davis. Pennsylvania M. J. **44:** 612–618, February 1941.

The shortcomings of intravenous urography definitely circumscribe its usefulness. It may be misleading for the following reasons: (1) An essentially normal pelvis may show a very poor filling. (2) A hydronephrotic pelvis may appear normal. (3) Of two hydronephrotic pelves, the one which is really the larger may appear smaller. (4) A hydronephrotic pelvis may show a very poor filling. (5) Cavities connected with the urinary tract but with no secreting elements may not show in the urogram. (6) Complete block of the ureter, whether of recent origin or long standing, prevents any delineation at all by intravenous urography. (7) Anatomic changes due to treatment may not be revealed.

(8) A normal ureter may not show at all. (9) A dilated ureter may appear normal.

Intravenous urography in the case of kidney tumor is, in the words of the author, "a waste of energy."

JOSEPH T. DANZER, M.D.

Indications for Excretory Urography. B. H. Nichols. Minnesota Med. **23:** 825–829, December 1940.

For excretory urography the optimum time for films after introduction of the dye is five, fifteen, and thirty minutes; after this a delayed film may be made at one hour. The contraindications for such examination are: (1) advanced renal dysfunction; (2) advanced cardiac decompensation; and (3) allergy to iodide salt. Urography is indicated (1) in cases of advanced prostatic disease where cystoscopy is impracticable or impossible and the study of delayed function is of great help to the surgeon; (2) in cases where it is impossible to catheterize the ureters; (3) in young patients and in the aged; (4) in the presence of hydronephrosis, nephroptosis, trauma to the kidney or ureters, and congenital anomalies; (5) in ureteral transplantations; (6) in the presence of vesical fistula, ureteral fistula, or vesical diverticulosis; and (7) in the presence of stone in the ureter or kidney.

A brief consideration of the diagnosis of the commoner urologic lesions follows, among which may be mentioned obscure backache in pregnancy and frequent urination in children. PERCY J. DELANO, M.D.

Kidney Tumours (An Analysis of a Series of 118 Cases). Emerson Smith and Allen Young. Canad. M. A. J. **44:** 149–152, February 1941.

The authors present an analysis of the renal tumors treated during the past twenty years in their service at Royal Victoria Hospital, Montreal. In this period 18,000 patients were admitted and 118 diagnoses of renal tumor were made; 21 of the 118 tumors were classified as benign, 97 as malignant.

Of the 21 benign tumors, 20 were operated upon. The findings were solitary cyst in 8 cases; multiple cysts in 2; fibroma in 2; papilloma and calculi in 2; papilloma (pelvis) in 3; hemangioma in 2; leiomyoma in 1. Most of the benign tumors, not including solitary cysts, were diagnosed as benign postoperatively. As far as the authors can ascertain, the 20 patients are cured.

Of the 97 malignant tumors, 62 were proved to be malignant by operation; 9 were not explored because of the patients' poor physical condition and 19 because of metastases; 7 patients refused operation. Sixty per cent of this group occurred between the ages of forty and sixty; 80 per cent occurred after the age of forty. There were 56 males and 41 females.

The sites of growth with the approximate percentage for each were as follows: upper pole, 25 per cent; lower pole, 18 per cent; middle area 16 per cent; total kidney, 25 per cent; kidney pelvis, 16 per cent. Clinically the picture varied from complete absence of urologic symptoms to combined gross hematuria, pain, and tumor. Hematuria was the most prominent initial sign, occurring in 50 per cent of the cases. Pain was the most prevalent symptom. The onset of symptoms before seeking medical attention ranged from ten hours to fifteen years. Two patients were admitted to the authors' service after operation elsewhere in the body, in one case in the skull and in one in the brain. The pathological reports suggested metastatic growths from the kidney. Thirty-one of the 97 cases showed metastases or direct extension into surrounding structures.

The history, physical examination, and cystoscopic and pyelographic studies usually furnished sufficient data to make an accurate diagnosis. Slight changes from normal noted in pyelograms may be difficult to interpret correctly. If diagnosis of a retroperitoneal mass is questionable, an exploratory operation is indicated.

Nephrectomy with removal of the involved lymph nodes offers the only hope of cure. If the growth has extended into surrounding tissues and is densely adherent, ligation of the ureter is to be considered. This controls pain due to passage of blood clots. Roentgen therapy may be used preoperatively, postoperatively, or both. Preoperative irradiation is particularly indicated in cases of Wilms' tumor. Prognosis is not encouraging, the ultimate mortality being given as high as 90 per cent by most observers. In the series reported the vast majority died from recurrences or metastases within five years, with an occasional survival of a few years longer.

The authors were impressed with the importance of an early diagnosis, the extreme malignancy of renal tumors, and the poor prognosis.

M. L. CONNELLY, M.D.

Malignant Renal Neoplasms in Children. C. C. Higgins and F. L. Shively, Jr. Arch. Surg. **42:** 386–394, February 1941.

This is a report on 26 cases of so-called Wilms' tumor. After a discussion of pathology, pathogenesis, and clinical signs, the roentgen diagnosis is covered rather fully. A large soft tissue shadow is found, which may displace the stomach and intestines away from it. Calcifications may be shown. Excretory urography often gives valuable information. Intravenous or subcutaneous injection of diodrast may be employed. Retrograde pyelography may be needed to secure a satisfactory study. While flattening of the pelvis and compression of the calices is typical, a normal pyelogram has been reported.

Certain other tumors, notably sympathetic neuroblastoma, may be difficult to differentiate. Polycystic kidney and large hydronephroses may be distinguished by pyelography.

Treatment is usually nephrectomy. Since this procedure is not always curative and since roentgen rays commonly cause the tumor to shrink markedly, preoperative irradiation is advocated. Roentgen therapy alone may occasionally produce a cure, but the results are inferior to those obtained by the combined attack. Newer apparatus and technics may bring about some change in this conclusion. LEWIS G. JACOBS, M.D.

THE SKELETAL SYSTEM

Spondylarthritis Ankylopoietica. C. L. Dunham and F. G. Kautz. Am. J. M. Sc. **201:** 232–250, February 1941.

The authors discuss the disease of the spine associated with the names of Bechterew, Pierre Marie, and Strümpell. They prefer, with others, to call it spondylarthritis ankylopoietica.

The involvement of the sacro-iliac joints, an essential part of the disease, may be the earliest and most characteristic sign. A spotty loss of contour of the joint surfaces, narrowing of the joint spaces, irregular areas of sclerosis in the ischia and pubes, with roughening of the periosteum, as well as "ulcerous" defects at, and bridging of, the symphysis pubis may occur.

The significant lesion in the spine itself is the involvement of the small posterior intervertebral articulations. The costovertebral joints may also be involved. In the early stages there is inflammation of the articular surfaces with exudation, invasion of cartilage by round cells, and fibrosis. As the disease advances, progressive destruction of cartilage occurs, and finally bony ankylosis. While all the joints are not involved simultaneously, the disease never remains localized to one or two joints. The formation of exostoses is rare.

An essential early change in the vertebral bodies is

a marked atrophy, without tendency to collapse. The discs are not involved, except perhaps in cases of long standing.

Calcification of the longitudinal ligaments usually follows the disease of the small joints, but these latter changes may occur in the absence of involvement of the ligaments.

The disease in the hips and shoulder joints resembles a severe atrophic arthritis. Occasionally, there have been considerable exostosis formation and calcification about the hip joints.

Spondylarthritis ankylopoietica is characteristically a disease of young male adults. The onset, usually insidious, may be preceded by any acute or chronic infection, or by acute or chronic trauma to the spine. Progressive stiffness may precede for a long time the occurrence of pain. Pain occurs first usually in the lower spine and sacrum, or occasionally in the neck. Many patients complain first of stiffness in the hips and legs. It has been pointed out that, because of the lack of definite objective findings, a diagnosis of malingering or neurosis is often entertained.

In a well established case there is rigidity of the spine, with loss of the normal lumbar lordosis and decreased expansion of the chest. Emaciation and loss of muscle tonus may be striking. The sedimentation rate is almost always far above normal during the active stages of the disease. Fever, leukocytosis, and anemia occur often and suggest the infectious nature of the disease. There is no concrete evidence that the gonococcus or the tubercule bacillus is the causative organism. This disease may be the spinal form of atrophic arthritis, but the occurrence of the spinal lesions for many years without involvement of the small joints of the extremities is opposed to this theory. The most frequent complications are pulmonary tuberculosis, iritis, pericarditis and pneumonia.

A diagnosis in the early stages can and must be made on clinical grounds, since roentgenographically demonstrable changes may take months or years to develop. The usual x-ray examination, including oblique views of the suspected area, will demonstrate the various stages of the disease. These range through decalcification and blurring of the joints, narrowing and finally obliteration of the joint spaces, and calcification of the ligaments. Except in older patients, in whom there may also be hypertrophic arthritis, the vertebral bodies and the discs are not involved.

In contrast with this disease, hypertrophic arthritis shows an onset of symptoms most often after the fourth decade; the sedimentation rate is not elevated, and fever and leukocytosis are uncommon. There is degeneration of the intervertebral discs with narrowing of the interspaces, formation of exostoses and wedging of the vertebral bodies in varying degrees. Bony bridging occurs in advanced cases.

General hygienic measures and a change to a warm dry climate are recommended. Symptomatic treatment directed against pain, anemia, and foci of infection is the rule. Intelligent conservative physiotherapy is of paramount importance. Orthopedic treatment is designed to relieve inflamed structures and prevent or correct deformities. BENJAMIN COPLEMAN, M.D.

Spondylolisthesis. Eduard Burckhardt. Schweiz. med. Wchnschr. **70:** 1093–1101, Nov. 16, 1940.

Spondylolisthesis and spondylolysis interarticularis are basically the same disease in different stages. For this reason the author prefers to term spondylolysis "spondylolisthesis imminens." This is believed to be a congenital condition; the theory of defective ossification of the arch is not opposed to this. Symptoms may appear spontaneously; sometimes they come after an accident, especially if sudden stretching of the back muscles has occurred. In two-thirds of the author's cases no preceding trauma was reported. The first clinical signs are often trifling. Stiffening of the back, low back pain, or radicular pains in the legs may appear, the last being due to interference with the nerve roots. For a definite diagnosis roentgenograms are essential; in frank spondylolisthesis the diagnosis is easy and a simple lateral view is enough. In spondylolisthesis imminens it may be difficult to demonstrate the changes. The lateral view alone is not always conclusive. Posterior and oblique views to show the articular processes may be needed.

In a series of 63 patients (37 men and 26 women) displacement of L5 (on the sacrum) was present 46 times, of L4 11 times, of L3 twice. Double displacements of L5 and L4 occurred 3 times, and of L3 and L2 once. Displacements of the fifth lumbar vertebra are of various degree, but those of the fourth never exceed 30 per cent. The angle between the axes of L5 and S1 measured longitudinally through the bodies was changed in proportion to the displacement; the normal average angle was 140°; that of the spondylolisthetic vertebrae was 160°. The angle of the inferior articular process with its body, normally about 115°, was increased to about 126° in spondylolisthesis imminens and to 140° in frank spondylolisthesis. The intervertebral space was in general narrowed in these cases.

The treatment recommended in adolescents is reposition of the displaced vertebra followed by an Albee-DeQuervain fusion to ankylose that portion of the spine. LEWIS G. JACOBS, M.D.

Cases of Spondylolisthesis of Unusual Interest. J. Blewett. Brit. J. Radiol. **13:** 416–421, December 1940.

Two cases of spondylolisthesis are recorded in which the condition could be demonstrated only by roentgenography in the erect posture.

SYDNEY J. HAWLEY, M.D.

Diagnosis of Marie-Strümpell Arthritis with Certain Aspects of Treatment. H. F. Hare. New England J. Med. **223:** 702–705, Oct. 31, 1940.

Within a two-year period, 21 cases of the Marie-Strümpell type of spondylitis have been seen at the Lahey Clinic. The etiology of this disease is unknown, but it attacks patients in their early twenties, especially males, beginning in the sacro-iliac joints and progressing up the spine. In the early phase, there are shifting pains in the arms, chest, and peripheral joints. Later, low backache occurs that is worse at rest and relieved by activity. The final stage is a stiff spine.

There is no characteristic roentgen finding in the earliest phase, but in the second phase of sacro-iliitis there is definite symmetrical sclerosis about the sacro-iliac joints with slight narrowing of the joint spaces. As the disease progresses, the apophyseal joints show narrowing or obliteration, there is decalcification of the vertebral bodies, and calcification of the spinal ligaments takes place. An increased sedimentation rate is a constant laboratory finding.

Hare is impressed with the high percentage of patients who are relieved of pain by roentgen therapy. Nineteen of the 21 patients here reviewed had returned to work. The technic is: 150–200 kv., 20 ma., 50 cm. distance, 0.25 to 0.5 mm. Cu plus 1 mm. Al, 300 sq. cm. field, and 300 r per dose per portal, per day The series may be repeated in three weeks. Relief of pain usually occurs in one to three weeks. Orthopedic exercises are also used. JOHN MCANENY, M.D.

Low Back Pain. H. W. Harris. J. Med. **21:** 469–471, January 1941.

In reviewing the anatomy of the lower back, accent is placed upon the lumbosacral joint because this is the change-over point from the flexible spine to the rigid

pelvis. The sacro-iliac joints are absolved of any but gross lesions because of their firm ligamentous and muscular support. In many instances of low back pain, the lumbosacral angle approaches a right angle and some men have brought about relief of pain by cutting the fascia lata or by stripping the muscle and fascia from the posterior iliac crests, either of which procedures permits the pelvis to rotate forward, resulting in less angulation at the lumbosacral junction. Rupture of the intervertebral disc frequently occurs at this site.

The lumbosacral joint should be thoroughly examined roentgenologically. First, a lateral film is made, with legs extended and the central ray directed along the superior surface of the sacrum. After this film is developed, the angulation necessary for the antero-posterior view can be determined. The joint is to be studied for symmetry, for the settling of the lumbar facets on the sacrum, and for arthritic changes. No mention is made of films in the lithotomy position or of oblique views for examining this region. Suggestions for treatment are included. JOHN MCANENY, M.D.

Fracture of the Column after Treatment of Psychoses with Cardiazol Shock. Agvald Vogt. Acta Radiol. **21:** 538–542, December 1940.

The author reports a series of 48 fractures in 20 patients following cardiazol shock therapy for psychoses. In all but 4 instances the thoracic vertebrae were the site of fracture. There were 3 fractures of the neck of the femur and humerus and one of the lumbar spine. The roentgen appearance, with wedge-shaped narrowing of the vertebral bodies anteriorly, suggests that the fractures occur during forward flexion, whereby the anterior edges of the vertebral bodies are pressed strongly against each other.

The author points out the necessity of roentgen examination before shock therapy to avoid confusion with old fractures or other lesions present before treatment. In patients with bone atrophy shock therapy is contraindicated.

For a further discussion of vertebral fractures after convulsive therapy and a bibliography, see Krause, G. R., and Langsam, C. L.: Radiology **36:** 725, 1941.

Mechanism of Post-Metrazol Gibbus. Thomas K. Rathmell. Pennsylvania M.J. **44:** 180–182, November 1940.

Radiographic changes due to the use of metrazol are divided into four classes: (1) lipping of the vertebral body with sclerosis; (2) lipping sclerosis and semilunar curving of the ventral margin of the vertebral body; (3) massive collapse of the body with or without sclerosis; (4) a combination of any of the above groups. There does not appear to be any correlation between the number of seizures and the radiographic changes.

The changes which are observed radiographically do not occur acutely and the author explains this fact by saying that, "during the period when hemorrhages and necrosis were widespread, as the result of the convulsive trauma, the supportive strength of the vertebral body was lowered. The convulsive seizures have resulted in a rupture of the disc and a fragmentation of the bone trabeculae. Subsequent compression of the vertebral body occurred due to the inability of such a fragile architecture to support the normal body weight." JOSEPH T. DANZER, M.D.

Transverse Process Fracture. L. Bayer. München. med. Wchnschr. **87:** 1394–1395, Dec. 13, 1940.

The author points out that fracture of a transverse process may be imitated by a number of anomalous conditions, and the mere association of an injury with a line on a roentgenogram is not of itself final. He illustrates examples of fracture, lumbar rib, and of a less common anomaly, a separate osseous structure at the tip of the last rib. LEWIS G. JACOBS, M.D.

Non-Traumatic Dislocation of the Atlantoaxial Joint. S. S. Hanflig and C. Schlosberg. New England J. Med. **223:** 713–716, Oct. 31, 1940.

This is a case report of a non-traumatic dislocation of the atlantoaxial joint. The seven-year-old patient had an upper respiratory infection with cervical adenitis, followed by a persistent torticollis. The atlantoaxial dislocation was not recognized, because of the difficulty of positioning the patient for radiography, until almost ten months had elapsed. Reduction was affected by manipulation under anesthesia.

The anatomy of the cervical region is reviewed. The etiology of non-traumatic dislocation of the atlantoaxial joint is not definitely known, but two theories are offered. One theory is that the transverse ligament of the atlas becomes relaxed, permitting dislocation to occur. The other is that, following hyperemia at the base of the skull, the bones become decalcified, permitting relaxation of joint capsular ligaments and slipping of the joint. The dislocation is always preceded by an upper respiratory infection.

JOHN MCANENY, M.D.

Anterior Dislocation of the Fourth Cervical Vertebra, Caused by Catatonic Posture of the Patient's Neck. N. J. Giannestras. J. Med. **21:** 484–485, January 1941.

This is a report of a patient seen and examined several times, who held his head in a flexed position and was suspected of having a cervical derangement of some sort. Repeated roentgen examinations showed no abnormality until two years after onset, when spastic paralysis of the right hand developed. At this time films showed a forward dislocation of the fourth cervical vertebra on the fifth. Reduction was only partially successful because of the condition of the patient.

JOHN MCANENY, M.D.

Use of Oxygen in Demonstrating Posterior Herniation of Intervertebral Disks. J. L. Poppen. New England J. Med. **223:** 978–982, Dec. 12, 1940.

Poppen discusses the development of myelography and the various contrast media used. He suggests the use of oxygen and describes the entire procedure.

The patient is prepared for spinal puncture on the x-ray tilt table with the more painful side up. With the head elevated, 40 c.c. of fluid is withdrawn from the spinal canal, the head is lowered to a 30-degree angle and a 50-c.c. syringe filled with oxygen is attached to the spinal needle and emptied. Stereoscopic lateral views are immediately made and then antero-posterior views. Fluoroscopy is impossible with oxygen.

Of 175 cases examined, 150 were proved at operation, and in only 5 of these was lipiodol required to clinch the diagnosis of herniated intervertebral disc. As experience broadens, more is seen in the films, and interpretation becomes more accurate.

JOHN MCANENY, M.D.

Treatment of Compound Fractures in War: Reports of Practical Experience in the Spanish Civil War. Leo Eloesser. J.A.M.A. **115:** 1848–1852, Nov. 30, 1940.

Rapidly moving warfare dominated by aviation makes simple surgical methods imperative.

The most satisfactory easily transportable and easily procurable skin disinfectant, both for the surgeon and the patient, is chlorinated lime.

It is seldom necessary to take an x-ray film of a compound fracture before débridement. Inspection of the limb before operation and of the fracture during

operation usually gives the needed information. Foreign bodies and the position of fragments are usually self-evident in the course of a proper débridement. Nor is it often necessary to take an x-ray film immediately after operation and immobilization if the operation is properly done and splints are properly applied. The time and place for x-ray examination are at the evacuation hospital and farther back, when fractured bone ends may have slipped or osteomyelitis and sequestration may be demonstrable.

The mobile surgical unit which the author headed in Spain was equipped with a good modern portable x-ray apparatus and a dark room but these were not once used. The same was true of other advanced units which he had occasion to observe.

It appears questionable whether its limited application in small advanced hospital formations, calculated for rapid movement and intense activity, justified the time, weight, bulk, and personnel needed to manage a portable x-ray unit. C. G. SUTHERLAND, M.D.

Fractures of the Tibial Condyles. E. M. Bick. J. Bone & Joint Surg. **23:** 102–108, January 1941.

In a group of 565 fractures of the tibia, 61 were fractures of one or both tibial condyles. These 61 cases were reviewed to determine the best results with respect to the function of the knee joint. In 22 cases the fracture was considered simple because of the mild disturbance as determined by x-ray. Treatment in 17 of these consisted in immobilization in plaster for from two to ten weeks.

The remaining 39 cases showed condylar displacement. Attempted replacement of the fragment by manipulation was unsuccessful. Of these cases, 31 were treated, as were fractures of the simple type, by immobilization in plaster, for six to seven weeks.

Complete follow-up is available in 33 of the 61 fractures, and function is surprisingly good. Early lateral instability of the joint almost invariably disappears in six to twelve months. Traumatic arthritis is noticeably absent, which is remarkable because most of these fractures occur in patients of middle life or beyond. The only frequent dysfunction noted was a limitation of flexion to 80 or 90 degrees, which tended to improve with time.

This study shows that operative replacement of depressed or fractured condyle is seldom necessary, and that conservative treatment in plaster produces good results in most cases. JOHN MCANENY, M.D.

Treatment of Fracture of the External Tibial Condyle (Bumper Fracture). Joseph S. Barr. J.A.M.A. **115:** 1683–1687, Nov. 16, 1940.

Of 75 consecutive examples seen of fracture of the upper end of the tibia, 30 (40 per cent) were fractures of the outer condyle without associated fracture of the fibula. Three types of injury account for these fractures: (1) a direct blow on the outer aspect of the knee, (2) a fall from a height, (3) a twisting injury. As the automobile bumper accounted for only 47 per cent of these cases, bumper fracture is not a particularly good name. The twisting injuries were all very similar, *i.e.*, the victim's foot during walking or running caught in a hole, and the sudden twisting violence transmitted to the knee caused the injury.

The degree of displacement of the fractured fragments is the key to rational treatment. Manipulation cannot possibly effect anatomic reposition of the joint surface of the tibia. An open operation is described that combines certain features of several previously described procedures and was believed to be the most satisfactory solution of the problem so far available.
C. G. SUTHERLAND, M.D.

Case of Fracture-Dislocation of the Mid-Foot with Reference to the Oblique Projection. Wilhelm Leun. München. med. Wchnschr. **87:** 1389–1391, Dec. 13, 1940.

The author reports a case in which following an injury to the left foot films taken in a hospital were reported as showing no bony injury. Only a single oblique projection was used. Persistent symptoms led to re-examination, at which time views in dorsoplantar, lateral, and posterior projections showed a downward, forward, and outward dislocation of the tarsal navicular with fracture of the cuboid. The author's oblique projection likewise failed to demonstrate the abnormalities. He concludes that it is poor all-round economy to take an insufficient number of films in any condition, and especially in industrial injuries. LEWIS G. JACOBS, M.D.

Growth of the Epiphyses. J. A. Siegling. J. Bone & Joint Surg. **23:** 23–36, January 1941.

Bone growth in the diaphysis has been proved to take place on the diaphyseal side of the epiphyseal plate. This is demonstrated by the appearance of transverse lines in the shaft caused by sickness and certain elements (phosphorus), and by the microscopic appearance of the columns of cartilage streaming into the diaphysis.

Information as to the growth of the epiphysis is in a confused state but if the same methods of investigation are applied to epiphyseal growth as are applied to diaphyseal growth it is seen that the dense lines in the epiphysis corresponding to the dense lines in the diaphysis arise in the articular side of the epiphysis and later new bone is formed just beneath the articular cartilage. Also, it is seen microscopically that the columns of cartilage extend into the epiphysis from the articular cartilage.

The question of nutrition of the epiphysis is believed to be settled by the fact that cartilage will continue to grow in synovial fluid, as is demonstrated in osteochondritis dissecans and in transplantation experiments.

Another proof of the active growth center in the epiphysis being on the articular side is demonstrated in a joint which is ankylosed by removing the articular cartilages of both surfaces of the opposing epiphyses. This has been done and the results show that the fused epiphyses do not change in depth.
JOHN MCANENY, M.D.

OBSTETRICS

X-Ray Pelvimetry for General Use. D. J. McSweeney and A. M. Moloney. New England J. Med. **223:** 1043–1049, Dec. 26, 1940.

The authors have devised a system of pelvimetry built upon the method of Ball that is simple, inexpensive, and practicable. Only anteroposterior and true lateral views of the pelvis are required to make the measurements, and the technic has been proved accurate by comparison with the Thoms and Ball methods. The exact contour of the inlet is not always defined, but if necessary a third view, with the patient in the semi-recumbent position, can be made.

This technic was used in a study of 200 unselected primiparae. The gynecoid type of pelvis was found in 65 per cent of the cases, the round type in 20 per cent, the android in 7 per cent, flat in 4.5 per cent, anthropoid in 3 per cent, and asymmetrical in 0.5 per cent. In only 20 per cent of the cases was the conjugata vera as determined by external measurements within 0.5 cm. of the measurement by x-ray, and in some instances there was a difference of 4.0 cm. or more.

The conjugata vera varied from 7.0 to 13.6 cm. All patients with a true conjugate of 9.5 cm. were delivered from below. The anterior and posterior sagittal di-

ameters of the inlet are computed, the latter dimension being of value in the android pelvis.

The transverse diameter of the inlet varied from 10.5 to 14.5 cm., the majority being over 12 cm. The bispinous diameter varied from 7.6 to 12.5 cm., the majority being 10 cm. or more. The narrow bispinous diameter was usually found in the pelvis of android tendency in the posterior portion of the inlet, and the funnel-shaped pelvis.

The posterior sagittal diameter of the mid-pelvis varied from 2.4 to 6.2 cm. This diameter is important to allow rotation of a posterior occipital presentation and for all practical purposes should measure at least one-third the bispinous diameter.

The pubotuberous diameter (perpendicular length of the fore-pelvis) varied from 6.5 to 10.8 cm. This diameter is of importance in the pelvis with a narrow subpubic arch and long pubotuberous diameter. Here an adequate bituberous diameter alone gives a false conception of the adequacy of the pelvis, because of its depth and narrow subpubic arch.

X-ray pelvimetry is indicated in primiparae at term in the presence of a floating head; multiparae with previous difficult labors; primiparous breech presentations; women with narrow subpubic arches and outlets; elderly primiparae with external conjugates of 18.5 cm. or less. JOHN MCANENY, M.D.

TECHNIC

Soft Tissue Radiography. E. P. Allen and H. W. Calder. Brit. J. Radiol. **13:** 422–427, December 1940.

Low-voltage radiography, though it produces a good film with excellent contrast, is not adequate to penetrate the denser structures. Therefore, in an adequately exposed film made with low voltage much of the soft tissue detail is lost if the denser structures are penetrated. Heavily filtered high-voltage radiation gives a better range of values. This is illustrated by sample exposures of a Benoist penetrometer and in actual radiographs. The author uses 4 mm. aluminum filter. This also produces a sharper image.

SYDNEY J. HAWLEY, M.D.

RADIOTHERAPY

MALIGNANT CONDITIONS

Pride and Prejudice in the Treatment of Cancer. Alfred Webb-Johnson. Brit. M. J. **1:** 1–5, Jan. 4, 1941; 39–44, Jan. 11, 1941.

This article (the Bradshaw lecture) constitutes a rather comprehensive address on the treatment of cancer and is of interest generally for its historical value and to the radiologist in particular in that it presents a sincere discussion of the relative merits of radiation and surgery in various forms of cancer. A high degree of respect for radium and x-ray is evident.

The author refers to the work of William Wood Bradshaw, who was intimately associated with the first special department for the investigation of cancer in Middlesex Hospital and to his own interest in this institution and the Holt Radium Institute. His response to the work of these schools is definitely optimistic. He notes a certain tendency to "exaggeration of the failures and overstatement of successes" and regrets that surgeons and radiologists are often in disagreement. He states that at present carcinoma of every part of the body except the stomach and intestinal canal has become a radio-surgical problem. He feels that there is much left to learn about radiation; that it is still frequently used for the reason that nothing else is available.

In discussing experimental cancer the three factors of inherent susceptibility, irritation, and virus infection are referred to. The first, it seems, is of prime importance; the other two are questionable. The problem in man is due to the fact that we have not the requisite knowledge as a guide in controlling susceptibility or increasing resistance. The work of the pathologist in determining the degree of virulence and radiosensitivity as well as making the diagnosis is praised highly. Early diagnosis is the key note in the successful treatment of cancer.

The comparative values of surgery and radiation are summed up something as follows: Radiation will cure a large percentage of skin cancers, but surgery is best where disfigurement may be avoided. Radiation gives the best results in lip cancer and cancer of the oral cavity. Cancer of the tongue calls for local radiation and operative removal of regional extension. In carcinoma of the larynx radiation is preferred. The subject of esophageal cancer is referred to without promise, though gastrostomy is mentioned as worth a trial. Carcinoma of the rectum is regarded as a surgical condition for the reason that the rectal mucosa is generally as radiosensitive as the tumor. Statistics covering carcinoma of the uterine cervix lead to the conclusion that better results are obtained by radiation than by surgery. The author draws no sharp distinction between radium and x-rays. Carcinoma of the breast is in the main a surgical condition. It is pointed out, however, that lumps which respond quickly to radiation in this region do not lend themselves well to surgical treatment and should be handled thereafter by radiation. The value of preoperative irradiation is held in doubt, but the use of x-rays in advanced cases is strongly advised.

The article closes with a discussion of the social aspects of the cancer problem as apparent in England, with comments on cancer centers, legislation, medical education, and research. Q. B. CORAY

Carcinoma in Young People and Its Treatment by Chaoul's Near Distance Roentgen Irradiation. W. Neumann. Strahlentherapie **68:** 509–517, 1940.

The author reports 17 examples of malignant growth in patients varying in age from eighteen to thirty years. These included 3 tumors in the rectum, 4 in the skin, 2 in the larynx, 3 in the breast, 3 in the parotid, and 2 melanomas. Of the 17 patients, 10 were symptom-free one to seven and a half years after treatment. ERNST A. POHLE, M.D., Ph.D.

Return to Normal Life of Patients with Distant Metastases as the Goal of Radiation Therapy. W. G. Deucher. Strahlentherapie **68:** 537–586, 1940.

The author undertook a statistical analysis of all tumor cases with distant metastases observed during the decade 1930–40 at the Roentgen Institute of the University of Zurich. A total of 432 cases were seen, 201 in males and 231 in females. The average age of all patients was 55.3 years; the youngest patient was one year old and the oldest one seventy-nine years. The majority of the metastases came from the primary tumor in the breast; next in frequency were cancers of the mouth and pharynx, followed by the thyroid, esophagus, stomach, and intestines. The results of the statistical studies are shown in numerous tables and graphs, which must be consulted in the original.

It appeared that the average duration of life of all irradiated patients from the time of the first distant metastasis was 15.6 months, with a normal life period

of 4.5 months. The respective figures for those who did not receive radiation therapy were 4.9 months and 0.5 month, proving beyond doubt the efficacy of the radiation. The author concludes that metastases in the lungs originating from embryonic tumor of the testicle, malignant struma, pleural metastases of all origins except the mouth, pharynx, and esophagus, should be irradiated. The same holds for bone metastases originating in thyroid, breast, testicle, and female genitalia, as well as skin metastases from any type of primary tumor if no other distant metastases can be found.

ERNST A. POHLE, M.D., Ph.D.

Experiences with Treatment of Carcinoma of the Face, Especially of the Eyelids, by means of Thorium-X. E. Saupe. Strahlentherapie **69:** 127, 1941.

The author relates his experience with interstitial thorium-x therapy practised by him and W. L. Meyer since 1926 and analyzes 66 cases of carcinoma of the face, in 25 of which the lesion was in the eyelid. There were approximately 12 per cent failures. From a technical standpoint it is interesting to note that the use of radium screens to protect the eyball had to be discontinued because of some undesirable complications. It was often possible to insert the seeds without anesthesia. The reaction subsides in six to twelve weeks. In an occasional case in which the implant was placed too close to the periosteum necrosis of the bone resulted, and this proved difficult to heal. Residual tumors are treated by additional implantations. Recurrences were observed in only 8 instances. The author points out that a recurrence can be simulated by a slow-healing radiation necrosis. ERNST A. POHLE, M.D., PH.D.

Carcinoma of the Breast in a Ten-Year-Old Girl. J. B. Sears and M. J. Schlesinger. New England J. Med. **223:** 760–761, Nov. 7, 1940.

The authors' ten-year-old patient with a mammary cancer is believed to be the youngest reported with this condition. It is very unusual to see carcinoma of the breast before puberty. A full report of the case is made with confirmation of the pathological diagnosis by Drs. Shields Warren, Charles F. Geschickter, Tracy B. Mallory, and Benjamin Castleman.

JOHN MCANENY, M.D.

Carcinoma of the Tonsil. L. Schönbauer. Strahlentherapie, **69:** 121, 1941.

The author presents an analysis of 104 cases of carcinoma of the tonsil treated at the Radiation Institute of the City Hospital in Vienna during 1931–38. The majority of these tumors were squamous-cell carcinomas. In the greater number interstitial radium therapy was used. Radium needles loaded with 2 mg. radium element distributed over 2 cm. length and with a wall thickness of 0.5 mm. platinum were inserted and left in place 72 to 100 hours; the dose per cubic centimeter of tissue was approximately 13 mg. hr. About one week later teleradium therapy over an area of 67 sq. cm., at 60 cm. distance, was applied, with a surface dose of 10,000–12,000 r. If the lymph nodes were enlarged they were removed four to six weeks after the treatment of the primary tumor had been completed.

The clinical material was divided into five stages. Not a single patient belonged to Group I. In Group II there were 6 patients, and of these 4 were still free from symptoms after six years; 2 after seven years. In Group III there were 21 patients with 11 free from symptoms. Group IV consisted of 48 patients with only 3 well up to one year. The remaining 29 were in an entirely incurable stage. The analysis shows that it is apparently possible to cure a carcinoma of the tonsil in the early stage.

ERNST A. POHLE, M.D., PH.D.

Primary Carcinoma of the Bronchus. Herman J. Moersch. Minnesota Med. **23:** 853–855, December 1940.

Primary bronchogenic carcinoma appears most often after middle age. The proportion of men to women is about 3:1. The onset if often insidious, and various pulmonary lesions may be simulated. The sputum, at first mucoid, later becomes purulent. Depending on the degree of obstruction and the virulence of the infecting organisms, bronchitis, bronchiectasis, pulmonary abscess, or gangrene may develop distal to the point of obstruction. Further increase in size leads to atelectasis. In 3 per cent of cases there have been no symptoms referable to the lung. When the tumor originates in the extreme apex of the lung, Pancoast has given it the name "superior pulmonary sulcus tumor" (see J.A.M.A. **99:** 1391–1396, 1932).

Carcinoma of the bronchus tends to metastasize early and widely. Metastatic nodes are found in about 20 per cent of the cases.

Differential diagnosis must include a consideration of dermoid, neurofibroma, foreign body, broncholith, lymphosarcoma, and tuberculosis.

Histologically the tumor is either a squamous-cell carcinoma or an adenocarcinoma, the former being slightly more frequent. The degree of malignancy is usually high.

Treatment depends upon the location, extent, and character of the tumor, the presence or absence of metastases, and the general condition of the patient. When possible, surgical diathermy applied through the bronchoscope for destruction of the tumor, followed by implantation of radium needles into its base, is recommended. If the location of the tumor forbids this, surgical extirpation is the procedure of choice. No cures are expected from roentgen therapy.

PERCY J. DELANO, M.D.

Medical Progress: Radiation Therapy in Gynecology. J. V. Meigs. New England J. Med. **224:** 67–72, Jan. 9, 1941.

The various methods of irradiation are discussed at some length as is also their manner of application.

Vulvar pruritus, vulvar leukoplakia, kraurosis vulvae, vulvar cancer, and carcinoma of the clitoris are all better treated by surgery. Some cases of carcinoma of the urethra are treated by irradiation and others by surgery. Endocervicitis is no longer treated by radium.

Cervical cancer seems to respond best to a combination of radium and x-rays. Many complications are known to follow irradiation. Vesicovaginal fistula may result from irradiation or from progression of disease. Rectovaginal fistula is less common, but does occur. Ureteral block may be due to fibrosis or involvement of the ureter by tumor growth. Intestinal obstruction is not uncommon following x-ray therapy and is due to fixation of the bowel at some point in the pelvis. Swelling of the leg may be due to recurrence in the broad ligament or pelvic fibrosis and lymphatic or venous block.

Carcinoma of the vagina is a difficult condition to treat. The prognosis is bad. The best results seem to follow radium and x-ray therapy. Vesicovaginal and rectovaginal fistulae occur.

Carcinoma of the endometrium is treated by a variety of methods. Irradiation of some sort is frequently used. Possibly the most widely employed treatment is irradiation followed by surgery. The disadvantage of intrauterine radium therapy lies in the difficulty of placing the radium in the proximity of the lesion, so that adequate dosage may be delivered.

Carcinoma of the fallopian tube is rare and the treatment is surgical.

In carcinoma of the ovary surgery is the proper treatment but x-ray therapy may be given after operation. Of patients with solid ovarian tumors about 9 per cent

survive five years; of those with papillary cystadenomata about 21 per cent live for five years.

Benign uterine bleeding occurring near the menopause should be treated by irradiation. Curettage should be done and radium placed in the uterine canal. In young women irradiation should be withheld unless no other means is found to control the bleeding.

Not all patients with fibroids should be irradiated; only those who have a symmetrical, smooth tumor no larger than a grapefruit. Fibroids occurring after the menopause should never be irradiated.

It is believed best to treat surgically all cases of endometriosis. Diagnosis should be confirmed by biopsy. If the condition is too extensive for surgery, irradiation may give relief.

Leiomyosarcoma of the uterus, although radiosensitive, should be treated surgically.

Sterility, amenorrhea, and abnormal bleeding may be treated by restricted irradiation.

JOHN MCANENY, M.D.

Development of Our Therapy of Carcinoma of the Uterus. A. MAYER. Strahlentherapie **69:** 17, 1941.

Originally the treatment of carcinoma of the uterus was entirely surgical. The mortality was fairly high, especially in patients with infected tumors. In an attempt to reduce the postoperative deaths due to peritonitis, preoperative irradiation was tried first in 1919 and proved so successful that it became a routine procedure. Postoperative irradiation increased definitely the percentage of cures. Since 1930 practically all patients have been treated by combined x-ray and radium therapy, but the details are not given. The author discusses briefly the methods for relieving pain in the advanced stage; also his follow-up system including social service work. He then considers the problem of euthanasia in hopeless patients but seriously doubts that this will ever be feasible. After all, he concludes, "it is the task of the physician to maintain life and not to destroy it." ERNST A. POHLE, M.D., PH.D.

Susceptibility of Carcinoma of the Cervix with Crater Formation to Radiation Therapy. W. HAUPT. Strahlentherapie **69:** 35, 1941.

From 1936 to 1940 the author saw 472 patients with carcinoma of the cervix. Seventy-eight, or 16.5 per cent were secondarily infected, with definite crater formation. Seventy-three of these were inoperable. Treatment was by radium, a total of 6,000 mg. hr. being given, distributed over three sittings of 2,000 mg. hr. each at 10- to 20-day intervals. Great care was taken to protect both bladder and rectum by means of wooden spacers. X-ray therapy was also given, in addition. The difficulties of radium application because of the presence of the crater and the uncertainty of the correct position of the screens are described. Five-year end-results are not available. The author presents as a preliminary conclusion that the primary response has been fairly satisfactory; if the applications are carried out carefully with smaller amounts of radium than in the uncomplicated cases of carcinoma of the cervix, healing of the crater takes place in about 80 per cent of the patients treated.

ERNST A. POHLE, M.D., PH.D.

Radium Therapy of Carcinoma of the Cervix During Pregnancy with the Aim of Delivery of Normal Offspring at Full Term. F. v. Mikulicz-Radecki. Strahlentherapie **69:** 45, 1941.

Carcinoma of the cervix developing during pregnancy is relatively rare. The author saw 5 cases of this type in his clinic and reports 2 in detail. The first patient was twenty-nine years of age and had radium therapy in the eighth month of pregnancy. Delivery was done by cesarean section followed by hysterectomy and deep x-ray therapy to the pelvis. The child now is two and a half years old and normal. The second patient was twenty-five years of age and had radium therapy during the seventh month of pregnancy. She received additional radium therapy two months following spontaneous delivery. Her child is now two years and three months old and also normal.

An attempt is made to calculate the doses of radiant energy reaching the fetal skull and it appears that these may be as high as approximately 3000 r. Although these two cases cannot be considered as final proof, they show that it is possible to irradiate carcinoma of the cervix during pregnancy successfully without injury to the offspring. ERNST A. POHLE, M.D., PH.D.

Results of the Treatment of Uterine Carcinoma with Roentgen Rays. H. Wintz. Strahlentherapie **69:** 3, 1941.

The author briefly reports his end-results in the treatment of uterine carcinoma with roentgen rays from 1915 to 1934. The percentage of five-year cures in a total of 1,636 patients was 19.6 per cent. Of the entire series, 226 were operable and among these the percentage of five-year cures rose to 61 per cent while for the 1,437 inoperable patients it dropped to 13.2 per cent. The respective figures for 261 carcinomas of the fundus were 42.9 per cent, with 69.1 per cent in 127 operable patients and 17.9 per cent in 134 inoperable patients. Adenocarcinoma of the cervix is reported separately because it is considered as more malignant; 52.9 per cent of 34 patients with operable lesions were free from disease after five years and 30.5 per cent of 59 with inoperable disease. It is worth while to note that 21 patients with carcinoma of the cervix lived for twenty to twenty-five years, 27 for fifteen to nineteen years, and 42 for twelve to fifteen years. Of those with carcinoma of the fundus 6 remained well for twenty to twenty-three years, 11 for sixteen to nineteen years, and 7 from twelve to fifteen years.

Additional figures are given for carcinoma of the breast, showing definitely the advantage of postoperative irradiation. The author considers sterilization by roentgen rays in women with carcinoma of the breast as a very important supplementary treatment.

ERNST A. POHLE, M.D., PH.D.

Results of Radiation Therapy in Carcinoma of the Cervix in the Women's Clinic, University of Munich, in 1934. H. Eymer and J. Ries. Strahlentherapie **69:** 12, 1941.

During the year 1934 there were observed at the Women's Clinic, University of Munich, 213 patients with carcinoma of the cervix. Of these, 206 were treated. After five years 77, or 36.15 per cent, were free from disease. The percentage of cures dropped from 71.43 per cent in Group I to 11.6 per cent in Group IV. Originally the method developed by Doederlein and Voltz had been used: irradiation of the hypophysis followed by x-ray therapy to the pelvis and then intrauterine, intracervical, and vaginal radium application for a total of 1,320 mg. hr. during a period of twenty-four hours. This was repeated eight weeks later but without irradiation of the hypophysis. Beginning in 1934 a third radium application was added with three-week intervals between the applications. X-ray therapy was administered after the first and third radium treatments. Since 1934 irradiation of the hypophysis has been discontinued. The authors conclude that radiation therapy of carcinoma of the cervix is the method of choice.

ERNST A. POHLE, M.D., PH.D.

Optimum Dosage in Treatment of Carcinoma of the Uterine Cervix by Radiation. M. C. Tod. Brit. J. Radiol. **14:** 23–29, January 1941.

The radiation dosage delivered to the parametrium was assessed in 370 cases of carcinoma of the cervix. Both over-dosage and under-dosage were found to produce unsatisfactory results. Though the number of cases is regarded as too small for more than tentative conclusions, this study seems to indicate that the optimum dosage is 7,500 to 8,500 r in six to seven days for radium only; 8,500 to 9,500 r in three to four serial weekly treatments by radium only, and 9,500 to 10,500 r for a total of combined radium and x-ray in four to six weeks' time. SYDNEY J. HAWLEY, M.D.

Radium Treatment of Cancer of the Penis. M. Lederman. Brit. J. Radiol. **13:** 393–409, December 1940.

Twenty-eight cases of cancer of the penis were treated by radium alone, with 61.9 per cent three-year survivals and 53.8 per cent five-year survivals. The technic of the treatment is described in detail. The complications are dysuria, meatal atresia, adhesive balanitis, penile atrophy, and hyperkeratosis.

SYDNEY J. HAWLEY, M.D.

Treatment of Leukemia by Radio-Active Phosphorus. S. Warren. New England J. Med. **223:** 751–754, Nov. 7, 1940.

The production of radioactive substances has brought to medicine both a new instrument for the treatment of disease and a tracer substance. Roentgen irradiation is considered sufficiently satisfactory in chronic leukemias, but is contraindicated in the acute and subacute stages. It was thought justifiable to submit cases of the two latter stages to treatment by radioactive phosphorus.

Phosphorus is activated by a cyclotron, changed chemically to a desired form, calibrated by a modified Lauritsen-type electroscope, diluted with glucose and saline, sterilized and injected intravenously in an appropriate quantity. It so happens that phosphorus is deposited in those tissues in which leukemic cells accumulate, namely, bones, liver, kidneys, and spleen.

Four case reports of acute and subacute leukemia treated by intravenous radioactive phosphorus are presented. In 2 some improvement was obtained as evidenced by the patient's general condition, the white cell count, and the condition of the bone marrow. In the other 2 the treatment was without significant effect. The author points out that this mode of therapy is still in an experimental stage and should not at present displace the more usual methods of irradiation in this disease. JOHN MCANENY, MD.

Reaction of Leukemic Patients to Sulfapyridine Administration. K. E. Livingston and R. D. Moore. New England J. Med. **223:** 975–977, Dec. 12, 1940.

Leukopenia following administration of sulfapyridine and related drugs has frequently been noted. Its effect in leukemia was observed in a patient with chronic lymphatic leukemia who developed pneumonia and was given sulfapyridine. The white count dropped sharply to normal and could be maintained at that level by continued use of the drug.

This phenomenon prompted further study on eight other patients. Some but not all cases of chronic lymphatic leukemia responded to sulfapyridine therapy with a fall in the lymphocyte count, but none of three cases of chronic myelogenous leukemia showed improvement.

The study is being continued in the hope that further investigation may identify related compounds more effective than sulfapyridine in producing this reaction.

JOHN MCANENY, M.D.

Hodgkin's Disease: Report of a Case with Unusual Longevity and Invasion of Heart and Pericardium. Max Ritvo. New England J. Med. **223:** 891–895, Nov. 28, 1940.

The case of Hodgkin's disease reported presents two unusual features: a survival of seventeen years after diagnosis and involvement of the heart. The survival is attributed to the judicious use of irradiation. At autopsy, a mass measuring 1.5 by 1.0 cm. was found in the heart extending through the wall and projecting into the right auricle. JOHN MCANENY, M.D.

NON-MALIGNANT CONDITIONS

Roentgen Near Distance Irradiation in Hemangioma. F. Schaefer. Strahlentherapie **68:** 518–521, 1940.

Since June 1939 the author has treated 52 angiomata in children from two to eighteen months of age by means of near distance roentgen irradiation. He applies 550 r (in air) per sitting and repeats this dose three or four times. The cosmetic results are as good as following radium therapy. Sixteen of the 52 patients were cured and 22 greatly improved; 14 had not responded well at the time of the report.

ERNST A. POHLE, M.D., Ph.D.

Roentgen Ray Therapy in the Treatment of Herpes Zoster. P. McCombs, A. Tuggle, and C. M. Guion. Am. J. M. Sc. **200:** 803–808, December 1940.

X-ray therapy was given a large group of patients with herpes zoster, with the following technic: 200 kv., 1 mm. of copper, and 1 mm. of aluminum filtration, 50 cm. distance, a 6 by 15 cm. portal directly over the spinal root ganglia of the involved segments; 200 roentgens were given every other day for five or six doses.

When comparison is made with the cases treated by other means, the detailed statistics clearly show a marked superiority in favor of x-ray therapy. Many more patients were cured, and the course of the disease was considerably shortened. The best results were obtained in the cases seen within one week after the onset of symptoms. The symptoms may be exaggerated after the first treatment. In order to guard against relapse a full course of treatment should be insisted upon, despite early relief of pain.

BENJAMIN COPLEMAN, M.D.

Radiation Treatment of Plantar Warts. J. H. Marks and C. C. Franseen. New England J. Med. **223:** 851–853, Nov. 21, 1940.

Plantar warts seem to be of more frequent occurrence than formerly, probably because of increased popularity of sports. They occur most frequently beneath the heads of the metatarsals, but may be found anywhere on the foot. They are painful, especially on direct pressure. The many methods of treatment attest the resistance of these lesions to cure.

A review of 175 cases disclosed that many plantar warts treated by irradiation were cured, but that undesirable results also occurred. The usual dosage of radium was up to 16 mc. hr. filtered through 0.3 mm. steel, with the area closely screened and the applicators applied to the surface of the lesion. When x-rays were used 1,200 to 1,800 r generated at 200 kv. with 0.25 mm. Cu and 2.0 mm. Al were administered. Oddly enough, the authors found repeated doses of 100 to 300 r sufficient to cure warts on the hands. Electrodesiccation is also advocated. JOHN MCANENY, M.D.

Treatment of Interdigital Epidermophytosis. du Bois. Schweiz. med. Wchnschr. **70:** 1223–1225, Dec. 14, 1940.

Although three types of Epidermophyton can be isolated culturally, the clinical lesions are indistinguish-

able. After some discussion of symptomatology and epidemiology, it is suggested that the first point in treatment is the use of a talc on the part to promote dryness. Applications of a 1 to 2 per cent alcoholic solution of iodine to the affected parts is good in chronic cases, but is inadvisable in the acute case. "Chrysophan" ointment sufficient to produce exfoliation may be used, but its application should not be entrusted to the patient. In the acute phases relief may be obtained by applying mildly antiseptic wet dressings under rubber dam. Ointments and pastes may reduce the inflammation but seldom result in a cure. Since the tenacity of the infection is directly related to the penetration of the mycelia into the skin, x-ray is a very desirable agent in all stages of the disease. The author believes that the application of a single "erythema" dose often results in a cure, but in the three weeks following treatment the part must be scrubbed with weak alcoholic iodine solution.

A rigorous course of procedure is recommended; a foot bath twice daily in 1/1000 potassium permanganate to which 20 gm. per liter of sodium chloride have been added; weak lysol may be substituted but sensitivity must be watched for. The parts are then freed of desquamated skin and scrubbed with a solution of acetone 0.2, metallic iodine 2.0 in 60 per cent alcohol to the desired strength. Finally the feet are dried and dusted with a powder consisting of equal parts of talc, zinc oxide, and bismuth subnitrate. The most important point is not to produce irritation with overtreatment.

LEWIS G. JACOBS, M.D.

Intensive Radiation in the Treatment of Hyperthyroidism. Roy G. Giles. Texas State J. Med. **36:** 675–678, February 1941.

The family physician is reminded that the results obtained by irradiation in hyperthyroidism are comparable with those obtained by any other method. It is believed that if patients realize this fact they will be less influenced by fear of surgery and will see their family physicians earlier, before cardiac damage has occurred.

Irradiation is indicated (1) if surgical treatment is contraindicated or feared; (2) in the presence of substernal goiter with hyperthyroidism; (3) when there are recurrent symptoms postoperatively, not controlled by iodine; (4) in children and adolescents with toxic diffuse or nodular goiters who do not respond to medical treatment; (5) for patients with mild symptoms who desire to avoid operation. Two hundred r are given to each side of the neck and posteriorly weekly for a total of 1,000 to 1,200 r, using 200 kv., 25 ma., 50 cm. focal skin distance, and a filtration of 1 mm. copper plus 2 mm. aluminum.

Statistics, opinions, and arguments are advanced to show that the objections to irradiation therapy are either unjustified in the light of present-day knowledge or merely theoretical.

JOHN M. MILES, M.D.

Radiation Treatment of Ganglia of the Wrist and Hand. F. M. Lyle. J. Bone & Joint Surg. **23:** 162–163, January 1941.

Ganglia most frequently occur about the wrist and produce pain, swelling, and weakness about the joint. Twenty-one patients have been treated by roentgen rays, the dosage being "1.5 erythema immediately over the tumor," repeated each month until the tumor disappeared, unless more than five treatments were necessary, when the interval was increased. (This is the only information given on dosage.)

Most cases needed only one treatment. One required 8 treatments. Eighty-one per cent of the tumors disappeared; 14 of 18 patients complaining of pain were relieved; 9 of 11 with weakness of the joint had return of normal function.

This method of treatment is believed to be best because of the high percentage of cures, the absence of scarring, and the avoidance of hospitalization.

JOHN MCANENY, M.D.

Treatment of Hemorrhage in the Climacterium with Special Consideration of Intrauterine Radium Therapy. H. Runge and A. Vöge. Strahlentherapie **69:** 82, 1941.

The authors present an analysis of 701 cases of climacteric bleeding observed at their clinic. They note that in 1935 there were 56 out of 70 cases treated with x-rays and 14 with intrauterine radium. This ratio was reversed in the following year, and in the last few years the majority of patients have been treated with radium; for the entire material the average ratio is approximately 3 to 1 in favor of radium. Following diagnostic curettage 2 radium screens of 25 mg. each are inserted in the uterus (0.6 mm. Ag filter) and left in place for forty hours. If x-rays are used four fields of 10 × 15 cm., two over the abdomen and two over the back, are exposed (180 kv., 40 cm. focal skin distance, 1.0 mm. Cu). The dose effective in the ovaries is approximately 300 r. A comparison of the two groups shows that in 92 per cent immediate amenorrhea occurred in those treated with radium as compared with 67.4 per cent in those treated with x-rays. One menstrual period occurred in 6.6 per cent of the radium and in 23.4 per cent of the x-ray group. The authors feel that there is less radiation sickness following radium application and that climacteric symptoms are less severe.

ERNST A. POHLE, M.D., PH.D.

Intrauterine Radium Treatment of Metropathia Hemorrhagica and of Uterine Fibroids. F. Siegert. Strahlentherapie **69:** 57, 1941.

The author discusses the mechanism of effect of x-rays and radium in sterilizing the ovaries. He points out that x-rays attack the ovaries directly, while following intrauterine radium application the changes in the endometrium are primary and those in the ovaries of an indirect or secondary nature, since very little radiant energy reaches the ovaries from the radium applicator placed in the uterus. Of 61 women treated with radium for metropathia hemorrhagica, 54 could be traced; there was no mortality due to the treatment. The dose varied from 1,200 to 1,500 mg. hr., with a filtration of 0.5 mm. brass. The treatment was successful in all cases except one, and in over 50 per cent the bleeding as well as menstruation stopped immediately. The influence of age was definite; of women between forty and fifty years, 63 per cent menstruated once or twice; but of those from 50 to 60 only 25 per cent.

Patients with uterine fibroids were treated with the same technic; the majority (75 per cent) were forty to fifty years of age. All 44 patients were cured; this exceeds the cures obtained with roentgen therapy (92.1 per cent). The author also has the impression that the climacteric symptoms following radium application are milder than after x-ray therapy and that there is less gain in weight after sterilization. Another advantage is the almost immediate cessation of hemorrhage. For very large and multinodular fibroids he advocates combined radium and roentgen therapy; 1,500 to 2,000 mg. hr. within the uterus and roentgen irradiation of the ovaries, 35 per cent H.E.D.

ERNST A. POHLE, M.D., PH.D.

Etiology and Therapy of Pruritus Vulvae. Alfred Labhardt. Schweiz. med. Wchnschr. **70:** 1212–1214, Dec. 14, 1940.

So-called pruritus vulvae is hardly more a disease than a cough or a pain. The itching is only a symptom. Its causes may be classified into four groups: (1) local vulvar irritation, including all sorts of inflamma-

tions, irritation from leukorrhea, uncleanliness, exanthemata, furunculosis, oxyuriasis; (2) endocrine malfunction, especially ovarian hypofunction; (3) toxic states affecting the skin, as in icterus or uremia; (4) nervous, psychic, and psychosexual traumata.

Cases in groups 1 and 3 are rare, and in group 4 not very common. Most of the cases observed by the authors were due to endocrine disease—practically always ovarian hypofunction. Of his last 50 patients, 15 were in the menopause; 26 below the menopausal age complained of oligo- or hypomenorrhea; 6 had normal or profuse menses, and 3 were pregnant.

Leukoplakia usually follows the onset of the itching, but may occasionally precede it. The malady is usually of long duration when medical advice is obtained. The itching is worse at night.

Hormone therapy in patients with ovarian hypofunction requires the use of folliculin to stimulate ovum production; the use of progestin, which produces maturation of the uterine epithelium, hardly enters into the picture.

In local irritative conditions the employment of Devegan or lactic acid douches (0.5 per cent) in conjunction with baths of aluminum acetate, liquor of lead subacetate, or witch hazel sitz baths is quite serviceable. Oxyuris infestation should be eradicated. In icterus and uremia the treatment of the primary condition is the only indication. Nervous, psychic, and psychosexual disturbances require psychotherapy. In administering hormones the most important point is the dose; small doses and oral administration are ineffective. In the menopause injections of 1 mg. estradiol three to four times a week followed by increasing doses up to 5 mg. and an intermission the last eight days of the cycle are indicated. Later the dosage may be slowly decreased.

As symptomatic measures, cool or cold sitz baths, anesthetic lotions or salves (10 per cent anesthesin ointment, nupercainal, calmitol) or a 1 to 2 per cent solution of phenol are helpful. Five per cent silver nitrate may be applied to the area once or twice a week. A paste of naftalan 20.0, zinc oxide and starch, each 10.0, is useful. Mesotan oil is not recommended. One can hardly expect much result from sedatives; narcotics are contraindicated.

Although roentgen irradiation is recommended in the literature, the author has never seen good results from it. Different authors prefer different technics, some advising unfiltered radiation, others filtered radiation. However, a dose of 50 per cent H.E.D. should never be exceeded for fear of late injury to the vulva. In earlier cases radical vulvectomy was employed, with results far from brilliant; this should be saved for a last resort. Resection of the pudendal nerve has been tried; also perineal injection of saline or anesthetic solutions. Of all these methods, the employment of hormone therapy in selected cases most recommends itself to the author. LEWIS G. JACOBS, M.D.

Radium Therapy of Induratio Penis Plastica. E. Günsel. Strahlentherapie **68:** 694–698, 1940.

The author relates briefly his experience with the treatment of induratio penis plastica by radium, reporting 2 cases. He constructed a special applicator consisting of a lead cylinder of 1 cm. wall thickness and 4 cm. inner diameter, around which 10 screens loaded with radium mesothorium (total 160 mg.) are arranged in such a manner as to permit homogeneous distribution of the radiation. His first patient received a total of 3,500 r on ten successive days; the second 4,000 r in ten sittings during fourteen days. In both patients there developed a rather marked reaction after three weeks and it is suggested, therefore, that the surface dose be reduced sufficiently to avoid any reaction in the skin.

ERNST A. POHLE, M.D., Ph.D.

TECHNIC

Some Advances in the Construction and Use of the Intracavity Cone. H. Martius and E. Witte. Strahlentherapie **69:** 29, 1941.

The authors have made some additional improvements in their body cavity tube, which is shown in several sketches. It is now possible to direct beams at 90 degrees or more to the tube axis. A detailed description of the construction is promised in the near future.

ERNST A. POHLE, M.D., PH.D.

Note on Dosage Data for Radium Therapy. T. H. Oddie. Brit. J. Radiol. **13:** 389–392, November 1940.

The dosage system of Paterson, Parker, and Spiers (see Brit. J. Radiol. **7:** 592, 1934; **8:** 155, 1935; **9:** 487, 1936; **11:** 252, 313, 1938) is extended to cover triangular surface areas and cones, prisms, pyramids, and tetrahedrons. SYDNEY J. HAWLEY, M.D.

EXPERIMENTAL STUDIES

Roentgen Therapy of Experimental Lobar Pneumonia in Dogs. L. M. Lieberman, P. J. Hodes and S. S. Leopold. Am. J. M. Sc. **201:** 92–100, 1941.

Lobar pneumonia was induced in the lower lobe of a lung in a number of dogs by means of intrabronchial injection of virulent pneumococci. None of the controls recovered. The irradiated animals were treated through a large lateral port, the rays being directed at the involved lung. One group was treated by 80 kv., another by 135 kv., and a third by 200 kv. roentgen rays. There were no recoveries in the first group, 1 out of 4 in the second, and 5 out of 13 dogs in the last.

The authors conclude that when sufficient dosage of radiation is used in the treatment of experimental lobar pneumonia in dogs there is definite evidence of a tendency toward recovery.

BENJAMIN COPLEMAN, M.D.

Treatment of Gas Gangrene Experimentally Produced. G. A. Caldwell. J. Bone & Joint Surg. **23:** 81–85, January 1941.

A culture of the Welch bacillus was implanted in wounds of guinea-pigs prepared by incising an extremity, drilling the bone, crushing and cutting muscle, and suturing the skin, in an attempt to produce conditions similar to a compound fracture infected with a gas-gangrene-producing organism.

Animals of one group were treated with 30 mg. sulfanilamide crystals placed in the wound. Fifteen of the 19 animals died. Nine animals, after débridement and irrigation, were given 50 mg. sulfanilamide intraperitoneally every six hours. Of these animals 7 lived and 2 died. Another group of five animals were treated by débridement, irrigation with saline, and instillation of zinc peroxide paste into the wound, with reopening of the wound in forty-eight hours and removal of the paste. Four of these animals lived. Ten animals were treated with a single dose of roentgen rays, 100 to 200 r, three hours after inoculation. Three of these animals survived. JOHN MCANENY, M.D.

Action of Dry Heat on Wood's Sarcoma. Kristian Overgaard and Harald Okkels. Acta Radiol. **21:** 577–581, December 1940.

Having found in experiments with a transplantable mouse sarcoma that heat had a specific tumor-destroying effect, the authors carried out a second series of experiments in which combined heat and roentgen therapy were used. A considerable increase in the percentage

of cures was obtained among animals which were given a slight heat treatment—42 or 43 degrees for five or ten minutes—either before or after irradiation (400–600 r). With the combination of the two measures, each in a dosage which must be considered therapeutically ineffective, a complete cure was obtained in many cases. Since it seemed to be a matter of indifference whether the heat treatment preceded or followed irradiation there would seem to be no question of a sensitization of the tumor cells to its effects. Furthermore, histologic studies seemed to indicate that the heat acts chiefly on other cell elements than those that are injured by the roentgen rays.

Action of Radiations Emitted by (1) Radium Plaques, (2) Unfiltered and Filtered Radon Seeds, and (3) Intravenous Injection of Radon Dissolved in Blood. A. Eidinow. Brit. J. Radiol. **13:** 357–370, November 1940.

The types of radiation mentioned in the title were tested upon rats and rabbits. The effects produced were the same for all and in both types of animal. Three hundred milligram hours from the radium plaque (filter 0.12 mm. Ag) are equivalent in effect to 2.5 millicurie seeds (filter 0.7 mm. Ag or 0.3 mm. Pt) and to 2.0 millicuries of radon dissolved in 0.5 c.c. of citrated blood.

Lethal doses produced death from toxemia. The fixed tissues showed degeneration, cloudy swelling, and irregular areas of hemorrhage. The endothelial cells were swollen and irregular and showed basophilic nuclei.

Irradiation *in vitro* did not produce death or change in phagocytic activity of leukocytes. *In vivo*, however, there was a pronounced fall in the number of white cells.

As it was thought that some toxic substance was formed in the skin, the skin areas that were irradiated were removed immediately after irradiation. This did not cause any change in the effects. The irradiated areas of skin were transplanted into unirradiated animals with no effect. Intravenously injected radon is carried by the blood to the fixed tissues, where it can be demonstrated by photographic and ionization methods. The constitutional effects were the same as with the other sources of radiation. Intravenous radon inhibited the growth of transplanted Watkins sarcoma. SYDNEY J. HAWLEY, M.D.

Studies Regarding the Course of the Radiation Reaction in Mouse Carcinoma Exposed to Roentgen Rays. W. Luther. Strahlentherapie **68:** 669–687, 1940.

The Ehrlich mouse carcinoma was exposed to roentgen radiation two and three weeks following transplantation. Seventy-six animals were irradiated and 25 served as controls; 50 and 90 kv. were used, with 11,000 and 4,000 r, respectively. The reaction was then studied microscopically. As criteria the author used the cell density per surface unit, the number of mitoses, the frequency of mitosis per thousand cell individuals, and the number of normal and injured cell divisions. It appeared that the course of the reaction in the carcinoma was dependent on the injuries to the chromosomes, which must be considered a secondary effect. The reaction curve of carcinoma treated with a single dose had the same shape as the curve obtained after fractional irradiation. A complete destruction of all cancer cells could not be accomplished even by a dose of 11,000 r. ERNST A. POHLE, M.D., Ph.D.

Further Lung Dusting Experiments. A. E. Barclay, K. J. Franklin, and M. M. L. Prichard. Brit. J. Radiol. **13:** 410–415, December 1940.

Finely powdered lead glass, bismuth carbonate, and finely divided carbon were introduced into cats' lungs by insufflation and inhalation. The dusts reached the alveoli in all subjects, though often not in sufficient quantity to be detected in the roentgenogram. The amount of alveolar dusting was not related to the amount in the bronchioles. Dusts collect in relatively greater amounts in inflamed areas of the lung.

The dust is excreted via the bronchi, being phagocytized by dust cells and carried out by the mucus current set up by the cilia and by coughing. Very little dust appeared in the lymph nodes.

SYDNEY J. HAWLEY, M.D.

MISCELLANEOUS

Influence of Radiation on the Electrolytic Coagulation of Mastic Sol. F. L. Warburton. Brit. J. Radiol. **14:** 30–35, January 1941.

Beta rays, ultraviolet rays, and x-rays in large doses coagulate certain colloids. The present experiments, done largely with beta and ultraviolet rays, were carried out to determine if small doses would sensitize the mastic sol to electrolytic precipitation. The relation between the log of the dose and the log of the time of coagulation follows a sigmoid curve, for which the equation is worked out. The similarity of these curves to the characteristic curves of photographic emulsions suggests that the action is a photochemical one.

SYDNEY J. HAWLEY, M.D.

A Long-Lived Isotope of Yttrium. Charles Pecher. Physical Rev. **58:** 834, November 1940.

With the 60-inch cyclotron at Berkeley, 16-million-volt deutrons were being used on strontium to produce the radioactive Sr^{89}. A by-product was a radioactive isotope of yttrium with a half-life of about a hundred days. With a thousand microampere-hours of bombardment the radioactive equivalent of 12 mg. of radium was obtained. This radioactive yttrium produces hard gamma rays comparable to the gamma rays from radium, but it is more expensive than radium for the same activity. R. R. NEWELL, M.D.